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A.M.A. Archives OF SURGERY

Parathyroid Crisis

Treatment by Emergency Parathyroidectomy

LT. CMDR. PHILIP R. JAMES
and
CAPT. PAUL G. RICHARDS (MC), U. S. N.

INTRODUCTION

Many excellent papers have been written in recent years on the subject of hyperparathyroidism, but there is little to be found in the literature regarding acute hyperparathyroidism or parathyroid crisis. A review of the available literature reveals only 14 cases to have been reported thus far, and in the majority of these the diagnosis was established only after the patient's death. Of the few cases in which the condition was diagnosed while the patient was still alive, in only two instances was the patient given the benefit of emergency parathyroidectomy. In this paper we should like to emphasize the importance of immediate surgery in the patient with hyperparathyroidism who develops an acute parathyroid crisis. We should also like to review briefly the cases reported and to point out their great similarity of symptomatology which should lead the physician to suspect that he is dealing with a case of acute hyperparathyroidism or parathyroid crisis, and, finally, to present a case of our own which was successfully treated by emergency parathyroidectomy.

Submitted for publication Aug. 29, 1955.

U. S. Naval Hospital, Corpus Christi, Texas.

The opinions or assertions contained herein are the private ones of the writers, and are not to be construed as official or reflecting the view of the Navy Department or the Naval Service at large.

REVIEW OF LITERATURE

The following cases of parathyroid crisis have been reported to date:

Dawson and Struthers (citing Oliver[1]) described, in 1920, the case of a man aged 49 who had had the typical bone lesions of hyperparathyroidism for many years. While under observation the patient had an acute syncopal attack and was admitted to the hospital in collapse, dying soon after admission. Autopsy showed a parathyroid tumor and extensive generalized calcification in the vessels, heart, lungs, stomach, kidneys, spleen, and liver. His collapse and subsequent death were thought to be due to parathyroid crisis.

In 1932, Lowenburg and Ginsburg[2] reported the case of a 5-year-old boy who, while under treatment for purpura hemorrhagica, was accidentally given 100 units of parathyroid extract daily for six days. On the second day of this therapy he began to vomit; listlessness was noted on the third day; severe depression developed on the fourth day, and by the fifth day he was critically ill, with a high irregular temperature up to 103 F. There was a marked apathy and absence of knee jerks. On the sixth day, his serum calcium was noted to be 19.6 mg. (as contrasted to 10.2 mg. per 100 cc. prior to admission) and serum phosphorus 4.4 mg. per 100 cc. Administration of parathyroid extract was immediately discontinued, and the patient's clinical condition and blood chemistry returned to normal promptly.

Hanes,[3] in 1939, described the case of a white housewife aged 49 who was admitted to the hospital complaining of pain in the

right chest and a feeling of fatigue. She had had pyelonephritis 11 years previous, and 5 years before a diagnosis of right hydronephrosis with calcareous deposits in both kidneys had been made. Her blood calcium at that time was 12 mg. and nonprotein nitrogen 50 mg. per 100 cc.; phenolsulfonphthalein excretion only 43% in two hours, and the urine contained hyaline casts and white and red cells. X-ray study of the kidneys showed diffuse calcific mottling of the parenchyma. The patient was admitted to the hospital approximately five years later with a one-year history of weakness and loss of weight. Physical examination was essentially negative except for a 2-cm. firm nodule at the left lower pole of the thyroid gland. X-rays of the kidneys were reported as follows: "The kidneys . . . are both filled with a mottled deposit of calcium typical of the changes seen in hyperparathyroidism. All of the bones show generalized loss of calcium." Blood chemistry on the fourth day of admission showed the calcium to be 20 mg. and phosphorus 4.7 mg. per 100 cc. Three days later the calcium was 22 mg. and phosphorus 4.8 mg. per 100 cc., phosphatase 23 Bodansky units, and plasma nonprotein nitrogen 58 mg. per 100 cc. Phenolsulfonphthalein excretion was 40% in 90 minutes. A diagnosis of parathyroid tumor was made, and the patient agreed to an operation. However, within a few days marked weakness and nervousness developed, her temperature rose to 101.3 F, the pulse was rapid, and the surgical consultant believed it advisable to postpone operation. Her condition rapidly deteriorated, and she died suddenly 11 days after admission. Autopsy showed a cystic, partly calcified and necrotic parathyroid tumor at the left lower pole of the thyroid gland and widespread calcification in the kidneys and myocardium, as well as calcium deposits in the stomach and lungs. Dr. Fuller Albright, in a personal communication to Hanes, commented that he believed the "patient died of parathyroid poisoning, which is a complication of hyperparathyroidism occurring when the blood calcium rises above a certain critical point. At this critical point the serum phosphorus, instead of being low, starts going up because phosphorus is no longer diffusible at very high levels of calcium."

Oliver,[1] in 1939, reported two cases of acute hyperparathyroidism, both of which terminated fatally. Case 1 was that of a 57-year-old woman who was admitted in a semistuporous condition, with complaints of nausea, retching, loss of weight, and drowsiness. During the preceding six months she had gradually lost 22 lb. in weight and had become increasingly weak. For two weeks she had had anorexia with nausea and retching when attempting to take solid food. The physical examination was essentially negative except for extreme drowsiness and a palpable tender left kidney. Urinalysis showed occasional red blood cells, numerous white cells, and hyaline and granular casts. Blood urea on the second and eighth days after admission was 76 and 136 mg. per 100 cc. respectively. The patient's course was steadily downhill with increasing stupor and a terminal rise in temperature and pulse rate. She died nine days after admission without developing localizing signs. On postmortem examination a chief-cell adenoma beneath the right inferior lobe of the thyroid gland was found. Necrosis and calcification were present in the kidneys, heart, stomach, lungs, and liver, and in the blood vessels of other organs. The blood calcium was 17.4 mg. per 100 cc.

Oliver's[1] second case was a woman aged 56 who was hospitalized for vomiting, loss of weight, anorexia, and pain in the chest of three months' duration. She had had similar symptoms one year before which cleared up after treatment and bed rest. On physical examination she was pale, and dehydrated, breathing deeply, drowsy, and vomiting repeatedly. There was a small tumor at the left lower pole of the thyroid gland which was thought to be a lymph node. The abdomen was tender throughout. Blood urea nitrogen was 176 mg. per 100 cc. A provisional diagnosis of uremia was made, but the patient became rapidly more comatose and died three days after admission before

more detailed investigation could be carried out. Autopsy disclosed a chief-cell adenoma of the left inferior parathyroid with widespread necrosis and calcification in the kidneys, lungs, heart, stomach, and visceral blood vessels.

In 1940, Smith and Cooke [4] reported the case of a 44-year-old woman who gave a history of dizziness and rheumatic symptoms for two years prior to admission to the hospital. A limp developed, the femurs became slightly bowed, and pain in the legs became severe. On admission she had abdominal pain, vomiting, and constipation. Urinalysis revealed albuminuria and a few red and white cells. Gastrointestinal x-ray series was negative. There was little change in the patient's condition until the 14th hospital day, when she became drowsy and incontinent. She deteriorated rapidly and died two days later. On the day of death, the blood calcium was 23 mg. per 100 cc. and the blood urea was 155 mg. per 100 cc. Autopsy showed a chief-cell adenoma of the right inferior parathyroid, osteitis fibrosa cystica of various bones, and calcinosis of the kidneys and pancreas.

In 1945, McClure and Lam,[5] in reporting the end-results in the treatment of hyperparathyroidism, describe the case of a 44-year-old white woman who sustained a pathological fracture of the femur. This lesion prior to fracture had been diagnosed as a metastatic malignancy because cytologic examination of the chest fluid was highly suggestive of a malignant process. After a course of deep x-ray therapy the patient developed a spontaneous fracture through the lesion. A consultant suggested the possibility of a parathyroid lesion and recommended surgical consultation. Two weeks later, a blood examination showed the calcium to be 19.4 mg. and phosphorus 3.88 per 100 cc. Persistent vomiting developed, the patient's temperature started to rise, and she went steadily downhill, dying six weeks after sustaining the pathological fracture. Autopsy showed diffuse hypertrophy of the parathyroids, calcification in the lungs, kidneys, and blood vessels and advanced osteitis fibrosa cystica of the bones.

Rogers, in 1946, reported two cases which appeared to be acute hyperparathyroidism associated with duodenal ulcer.

Case 1 was that of a 36-year-old Negro man who was admitted to the Mayo Clinic in 1943 with a seven-year history of intermittent epigastric pain. A gastrointestinal series revealed a duodenal ulcer without obstruction. The patient was placed on an ulcer regimen, which relieved the pain but which was followed by the onset of vomiting after several days. This sequence occurred on two additional hospitalizations, in July and August, 1944. On Aug. 29, 1944, the patient became comatose and developed a rectal temperature of 105 F.[6] Marked oliguria and azotemia ensued, and he died two days later.

Significant postmortem findings were a $3 \times 1.5 \times 1.7$ cm. chief-cell adenoma of the right inferior parathyroid gland, a healed duodenal ulcer, and widespread calcium deposits in the lungs, kidneys, and small arteries.

Case 2 was that of a white man 53 years of age who was admitted to the Mayo Clinic on June 4, 1945, with a two-year history of epigastric pain and vomiting. An upper gastrointestinal series revealed a duodenal ulcer without gastric retention. The patient was placed on an ulcer regimen, with control of the pain, but after three days vomiting became severe. Because of failure to improve, subtotal gastric resection was done. Persistent vomiting recurred postoperatively. On July 9, he became semicomatose and went into shock. On July 10, he sank into coma and developed a temperature of 106 F terminally. Blood study revealed a urea nitrogen of 232 mg. per 100 cc.

Significant postmortem findings were primary hypertrophy of the parathyroids and supernumerary parathyroid glands and metastatic calcification in the kidneys and dura mater.

Waife,[7] in 1949, reported five cases of acute hyperparathyroidism. Only two of

these were undoubted instances of acute primary hyperparathyroidism, both due to adenoma. Case 1 was that of a 50-year-old Negro man, previously entirely asymptomatic, who suddenly developed severe abdominal pain and vomiting, followed by weakness and lethargy. After a fracture of the patella on the ward, he was found to have hyperparathyroidism, as evidenced by a blood calcium of 17.5 mg. per 100 cc., a blood phosphorus of 1.8 mg. per 100 cc., and osteitis fibrosa cystica. At operation one month later two small parathyroid adenomas, 1 cm. in diameter, were found and removed. The Sulkowitch test was strongly positive 12 days after operation, showing that, unfortunately, the metabolic disorder was not relieved. The author postulates that the extremely rapid onset of symptoms suggested that the patient's calcium level may have suddenly reached the "toxic" level, inasmuch as the bone changes indicated that the disease had been present for some time.

Waife's [7] other case of apparent acute primary hyperparathyroidism was that of a 44-year-old man who 4 years previously had developed bilateral sacroiliac pain associated with epigastric pain and vomiting. One year later he developed severe cramps in both calves and later had abdominal and arm cramps. Eight months before admission to the hospital all symptoms became marked. Physical examination revealed an acutely ill, prostrated white man; occasional muscle twitches and exaggerated reflexes were noted. Blood examination revealed nonprotein nitrogen between 50-90 mg. per 100 cc., serum calcium of 19.3 mg. per 100 cc. and serum phosphorus of 4.3 mg. per 100 cc. The phenolsulfonphthalein excretion was impaired. Urinalysis showed a 3+ to 4+ albuminuria, a few red blood cells, and hyaline casts. A gastrointestinal series showed a persistent duodenal deformity. X-rays of the kidneys revealed a group of calcified bodies in the region of the left kidney. Osteoporosis of the tibia, radius, and ulna was present. A diagnosis of hyperparathyroidism was made, and at surgical exploration an adenoma of one of the parathyroids on the right was removed. The pathological report was that the cells were "wasserhelle" in type, having "arisen entirely from the chief cells." Postoperatively the serum calcium and phosphorus returned to normal. Five years later, suffering from hypertension and renal insufficiency, the patient developed an aortic aneurysm which dissected and ruptured into the pleural cavity. Necropsy revealed calcification in the kidneys and lungs. The renal insufficiency second to hyperparathyroidism was partially relieved by operation in this case, but it eventually led to severe hypertension and death.

In 1950 Staub and co-workers [8] described the case of a man aged 50 who was admitted to the hospital three months after the accidental discovery on routine chest x-ray of a mass in the left anterior mediastinum. For the past year he had noticed general weakness, lassitude, and easy fatigability. He had had a cough for three months, low back pain, and drawing sensations in his knees. Physical examination was essentially negative. The clinical impression was a mediastinal tumor, for which he received 2000 r of x-ray over a period of five days. During the last two days of this therapy he complained of weakness and anorexia and began to vomit frequently. A blood examination done four days prior to the onset of the x-ray therapy showed 14.1 mg. of calcium and 2.1 mg. of phosphorus per 100 cc. His course continued downhill and he suddenly died on the 28th hospital day, 8 days after his last x-ray treatment. Autopsy revealed a cystic tumor in the mediastinum 7 cm. in diameter, which on the microscopic examination proved to be parathyroid tissue, mostly chief cells. There were also numerous foci of calcification. The authors believed that acute parathyroid intoxication was probably the cause of death.

Kretschmer,[9] in 1950, reported the case of a 35-year-old woman who seven years previously had passed a kidney stone after a typical attack of left renal colic. Subsequently

she had 75 cystoscopies and approximately 20 attacks of renal colic during a two-year period, calculi being passed in half of these attacks. One week prior to her last admission to the hospital she had severe attacks of pain, nausea, vomiting, belching, and frequency and stiffness of the hips, shoulders, and knees. A palpable mass was found over the right lobe of the thyroid gland and was diagnosed as an enlarged parathyroid. Blood chemistry revealed a nonprotein nitrogen of 44 mg. calcium of 16.3 mg., and phosphorus of 2.6 mg. per 100 cc. X-ray showed multiple calculi in both kidneys. She was cystoscoped four days after admission, and 11 hours afterward there was noted marked lassitude, great fatigue, and pain in both knees. The day of cystoscopy she suddenly went into profound shock, for which she was given 500 cc. of blood and 500 cc. of plasma without effect. On the next day adrenal cortical extract was given, without benefit. The following day her temperature was 102 F and nonprotein nitrogen 80 mg. per 100 cc. On the fourth day after cystoscopy her blood pressure was 78/70, and when the cuff was inflated tetanic contractions in the arm developed. Her temperature rose to 103 F rectally, and she died two hours later. Postmortem findings were parathyroid adenoma; bilateral renal calculi; acute and chronic bilateral pyelonephritis; left hydronephrosis; subarachnoid hemorrhage; passive congestion of the liver, spleen, and kidneys, and acute gastritis. The bones were normal. The author states, "The possibility of an acute hyperparathyroid crisis was considered in this case."

In 1953, Schneider [10] reported the case of a 58-year-old man who was admitted to the hospital for a fracture of the right femur sustained when he tripped over a rug. After one week in bed in traction, he began to have persistent vomiting and weakness and his voice became barely audible. His family said that weakness had begun five years before and had lately become extreme. He had also had a mass in the neck for several years which was presumed to be a simple colloid goiter. The mass had increased in size during the two months prior to admission. There was also a history of anorexia, muscle cramps, loss of stature, and loss of weight for several years. On physical examination there was generalized muscular hypotonicity and a cyst-like mass 12×10 cm. in the neck, which felt like a colloid goiter. The chest was "pigeon-breasted with a striking concavity in the lateral dimensions." A cystic lesion was present by x-ray in the second and third metacarpals. The tendon reflexes were barely obtainable. A blood examination done on the 9th hospital day revealed a serum calcium of 29 mg. per 100 cc., phosphorus of 2.1 mg. per 100 cc., phosphatase of 13.6 Bodansky units, and a urea nitrogen of 66 mg. per 100 cc. With the established diagnosis of hyperparathyroidism, the patient was treated as a surgical emergency and operated on the following morning. A large parathyroid tumor was removed (cystic adenoma of left inferior parathyroid). The patient who seemed to be moribund prior to surgery made a swift recovery.

Thus, there have been reported so far 14 cases of acute parathyroid intoxication of which one was due to the accidental administration of parathyroid hormone. Eleven cases were due to parathyroid adenoma and two cases to diffuse hypertrophy of the parathyroids. Conceivably the dearth of medical literature concerning this particular aspect of hyperparathyroidism has resulted in a failure in many cases to consider the possibility of parathyroid crisis, thus depriving the patient of what may well be a life-saving procedure, viz., emergency parathyroidectomy. The following is the report of a case of parathyroid crisis successfully treated by emergency parathyroidectomy.

REPORT OF A CASE

A 22-year-old white woman was admitted to the hospital on Aug. 17, 1954, after a routine physical examination had revealed a hypertension of 170/100 mm. Hg. The past history was not unusual until approximately 13 months preceding her admission. During this period she had been seen by several physicians because of a multitude of complaints,

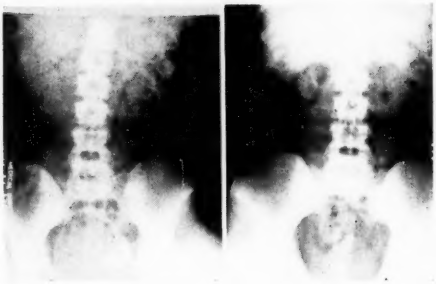

Fig. 1*A*.—Flat film of abdomen 10 days prior to surgery, showing calcific deposits in region of right kidney. Intravenous pyelogram demonstrated right nephrolithiasis. (Official U. S. Navy photograph.)

Fig. 1*B*.—Flat film of abdomen six months after operation showing marked diminution in amount of right nephrolithiasis. (Official U. S. Navy photograph.)

including at various times anorexia, nausea, occasional vomiting, epigastric discomfort, and aching pains in the bones of the lower extremities. The patient had remarked on one occasion after being on her feet that she was "unable to touch" the bones because of the pain, especially about the ankles and along the tibia. She had also noticed polydipsia and polyuria for approximately 10 months.

Physical examination revealed a well-developed and nourished woman who appeared somewhat pale but neither acutely nor chronically ill. The blood pressure on admission was 130/86 mm. Hg. The pulse was 84 and the temperature was normal. Except for a nodule about 1-1.5 cm. in diameter in the inferior aspect of the right lobe of the thyroid gland, physical examination was entirely normal.

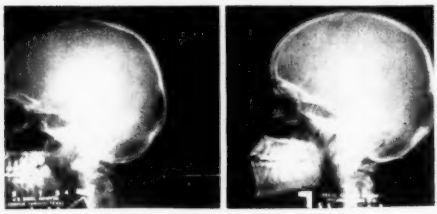

Fig. 2*A*.—Skull film taken three days prior to operation, showing diffuse granular decalcification. (Official U. S. Navy photograph.)

Fig. 2*B*.—Repeat skull film five and one-half months after operation, showing definite recalcification. (Official U. S. Navy photograph.)

Intravenous phenolsulfonphthalein excretion tests disclosed a rather marked functional impairment. Maximum urinary concentration on two occasions was 1.011 and 1.012, respectively. Flat film of the abdomen disclosed right nephrolithiasis (Fig. 1*A*). A random urine specimen revealed a strongly positive Sulkowitch test. Other pertinent laboratory data are recorded in Tables 1 and 2.

The history, marked impairment of renal function, nephrolithiasis, and hypercalciuria suggested the possibility of hyperparathyroidism. Subsequent blood chemistry studies revealed hypercalcemia and hypophosphatemia. Dental x-rays revealed a normal lamina dura. Skeletal survey disclosed a diffuse but minimal demineralization, most apparent in the skull, tibia, and humeri (Fig. 2*A*).

The patient remained completely asymptomatic during the first two weeks in the hospital. On the evening of the 15th hospital day, the patient began to complain of epigastric distress, nausea, and anorexia. During the next 36 hours, the epigastric

TABLE 1.—*Laboratory Data—Blood Chemistry*

Date	Calcium, Mg/100 Ml.	Phosphorus, Mg/100 Ml.	Alkaline Phosphatase, Bodansky Units	Total Protein, Gm/100 Ml.	Blood Urea Nitrogen, Gm/100 Ml.	Chloride, mEq/L.	Potassium, mEq/L.	CO_2 mEq/L.
8/26/54	8.0	...	11.0	...	20.3	....	....	....
9/ 2/54	15.0	1.8	...	6.0	....	....	....	....
9/ 4/54	Day of operation							
9/ 4/54	17.0	...	...	...	20.8	72.4	....	35.5
9/ 5/54	13.6	...	...	...	82.5	....	2.75	....
9/ 7/54	6.5	1.8	3.3	...	16.7	....	2.9	29.2
9/ 9/54	7.5	2.4	...	...	....	....	....	....
9/10/54	10.0	3.2	...	...	22.0	103	....	....
9/13/54	9.0	4.1	...	6.6	14.8	....	4.7	....
9/20/54	9.0	3.1	...	...	....	....	....	....
9/27/54	9.6	...	7.6	...	....	....	....	....
10/ 4/54	10.4	3.8	5.3	...	....	....	....	....
10/19/54	11.2	4.0	...	...	....	....	....	....
11/16/54	10.4	...	...	...	....	....	....	....
1/ 7/55	9.2	3.8	...	...	....	....	....	....
2/12/55	9.2	3.2	4.9	...	15.3	....	....	....

pain became severer and was only partially relieved by atropine and meperidine (Demerol) hydrochloride. During the early morning hours of the 17th day, the nurse on duty noted extreme restlessness and had difficulty in counting the pulse accurately. The pulse was thready and appeared to show extreme variations in rate, with values of 38 to 160 recorded by the nurse. Later that morning the patient's condition became critical. Her pulse and blood pressure were difficult to determine. She was unresponsive to painful stimuli, moaned constantly, and showed marked restlessness, with continual movement of the arms and legs. Soon thereafter the patient lapsed into deep coma, showed cyanosis, and developed a rectal temperature of 105 F. There was peripheral vascular collapse, and the pulse and blood pressure were unobtainable.

blood pressure was faintly audible at 100/80 mm. Hg and the temperature had declined to 100 F rectally. In spite of the continued administration of levarterenol, the blood pressure and pulse were weak and unstable. A serum calcium determination done at this time was found to be 17 mg. per 100 cc. In spite of the critical condition of the patient it was believed that parathyroid exploration, with removal of a hyperfunctioning adenoma, if present, offered the only hope of arresting the acute course of her disease.

Emergency surgery was performed on the evening of the 17th day with light thiopental (Pentothal) sodium and local anesthesia, with levarterenol being administered intravenously to maintain the blood pressure. The previously noted nodule in the right lobe of the thyroid was found to be a solitary

TABLE 2.—*Miscellaneous Laboratory Data*

	Blood			Urine					Phenolsulfonphthalein Test (I. V.)	
Date	R. B. C.	W. B. C.	HgB.	Specific Gravity	Albumin	Sugar	Calcium (Sulkowitch)	Microscopic Examination	15 Min.	120 Min.
8/18/54	.....	8,200	11.5	1,010	Neg.	Neg.	.....	Neg.	....	....
8/21/54	.....	.....	....	.....	.....	.....	.....	.....	5%	30%
8/26/54	.....	.....	....	.....	.....	.....	++++	.....	....	....
9/ 1/54	.....	.....	....	.....	.....	.....	.....	.....	4%	30%
9/ 4/54	Day of operation									
9/ 4/54	4,790,000	27,750	11.0	Qns.	20 mg.	Neg.	++++	8-10 RBC/HPF	....	....
9/ 5/54	.....	28,800	12.5	1,014	10 mg.	Neg.	++	.....	....	....
9/10/54	.....	11,550	9.5	1,010	Neg.	Neg.	++	6-8 RBC/HPF Occasional WBC	....	....
9/23/54	.....	7,500	11.0	.....	.....	.....	.....	.....	....	....
9/27/54	.....	.....	....	1,027	Neg.	Neg.	++	Neg.	....	....
10/15/54	.....	.....	....	1,021	Neg.	Neg.	+	Neg.	30%	75%
1/10/55	4,430,000	11,050	12.5	1,025	Neg.	Neg.	.....	Neg.	20%	65%
2/12/55	.....	8,000	11.0	1,020	Neg.	Neg.	++	Neg.	....	....
2/18/55	.....	.....	....	.....	.....	.....	Neg.	.....	20%	65%

The explanation of the patient's acute symptoms was not fully appreciated initially. The close similarity of her clinical picture with that of an acute adrenal insufficiency prompted therapeutic measures to combat this possibility. Emergency measures consisted of oxygen through a nasal catheter and 5% dextrose in saline with 8 mg. of levarterenol (Levophed), given into the femoral vein while venous cutdowns were being done on both lower extremities. During the next three-hour period, the patient was given 50 cc. of aqueous adrenal extract; 300 mg. of cortisone acetate intramuscularly, 500 cc. of type O negative whole blood, and 400 mg. of intramuscular tetracycline (Achromycin) hydrochloride. Throughout the entire period continuous infusions of both levarterenol and hydrocortisone were administered. Approximately three hours after the institution of these measures, the adenoma of the thyroid gland. Further exploration revealed an adenoma of the right superior parathyroid, which was lying in a sulcus on the posterior aspect of the upper lobe of the thyroid in close proximity to the recurrent laryngeal nerve. This tumor was excised. Because of the critical condition of the patient the thyroid adenoma was not removed at the same time.

Postoperatively the patient showed gradual improvement. Her pulse and blood pressure began to stabilize, although it was necessary to continue a slow drip of levarterenol for 10 hours following surgery. The patient was maintained on a continuous intravenous infusion of calcium gluconate for the first three days after surgery; mild tetanic reaction developed if this was discontinued. She regained consciousness about 12 hours after surgery. During the 10-hour interval between the onset of

Fig. 3.—Gross photograph showing typical encapsulated lobulated structure. (Official U. S. Navy photograph.)

the acute crisis and the operation and for 12 hours postoperatively, the patient showed a marked oliguria. However, during the second 12-hour period postoperatively she had a renal output of 1500 cc. The intake for the same period was approximately 2000 cc. of intravenous fluid. The patient was placed on a high-calcium, low-phosphorus diet on the fourth postoperative day. In addition she was given vitamin D, 50,000 international units three times daily, and large doses of calcium lactate for three weeks after surgery. The Chvostek sign was positive until the 14th postoperative day. Serum calcium determinations during this period were in the low normal range, and Sulkowitch tests for urinary calcium were faintly positive. An upper gastrointestinal x-ray study done later in the hospital course was normal. The patient improved rapidly after the first three weeks. On Jan. 14, 1955, excision of the thyroid adenoma was accomplished by means of a right lobectomy. This tumor was found on microscopic examination to be a colloid adenoma. Convalescence was uncomplicated.

Renal function studies performed three to five months after parathyroidectomy disclosed striking improvement. Random specimens revealed a specific gravity varying from 1020 to 1027. Phenolsulfonphthalein excretion tests revealed remarkable improvement in comparison with those performed preoperatively (Table 2).

Repeat skeletal x-rays revealed evidence of recalcification, which was quite apparent on the skull films (Fig. 1*B*). There was a definite decrease in the degree of nephrolithiasis (Fig. 2*B*). Numerous serum calcium and phosphorus determinations were normal.

For at least 10 months prior to operation this patient had experienced signs and symptoms referable to the three systems classically involved in hyperparathyroidism: gastrointestinal, renal, and

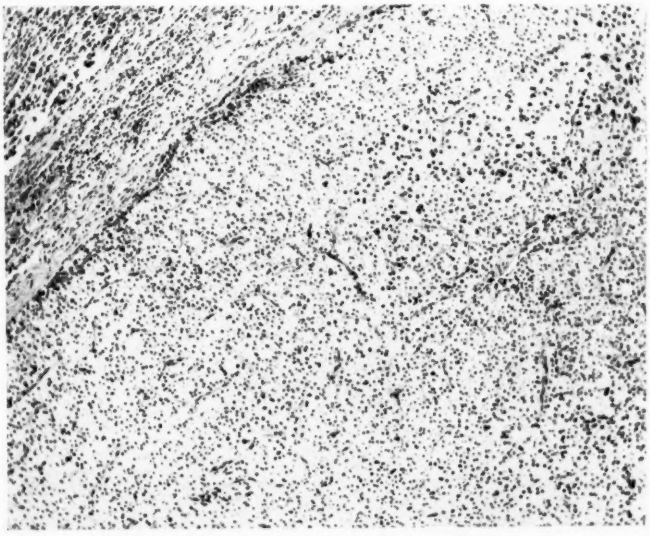

Fig. 4.—Low-power photomicrograph of the tumor showing the encapsulated adenoma composed principally of chief cells. Remnants of compressed normal parathyroid tissue are seen beyond the capsule at upper left. Hematoxylin and eosin stain; × 90. (Photomicrograph, courtesy Armed Forces Institute of Pathology, Washington, D. C.)

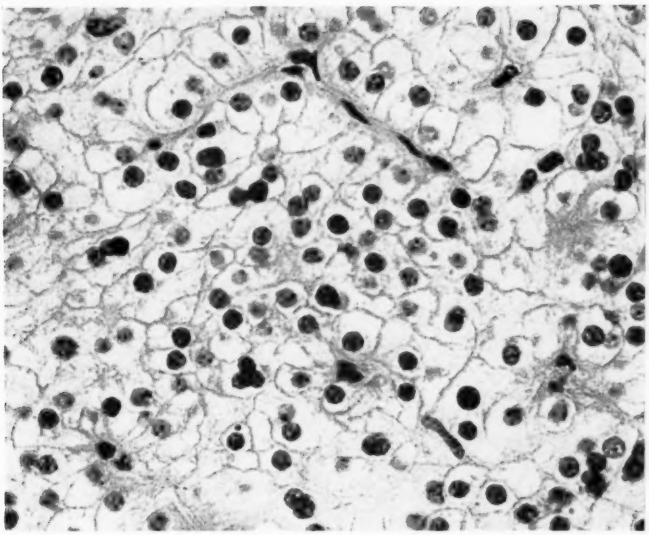

Fig. 5.—High-power photomicrograph of the tumor showing typical large adenoma cells with their sharp cell borders, clear cytoplasms, and small round nuclei. Hematoxylin and eosin stain; × 650. (Photomicrograph, courtesy Armed Forces Institute of Pathology, Washington, D. C.)

skeletal. Since operation she has regained 15 lb., the polydipsia and polyuria have subsided, and she is completely asymptomatic.

Pathological Reports.—

Sept. 4, 1954: Specimen. Adenoma of parathyroid gland (Figs. 3, 4, and 5).

Gross. Specimen consists of an encapsulated, roughly kidney-shaped mass of tissue measuring 2.7×1.7×0.8 cm., weighing 2.35 gm., and firmly lobulated. On cross section it has a white appearance.*

Microscopic. Sections show masses of parathyroid cells, mostly of the chief-cell variety, embedded in a vascular reticular network. The tumor is encapsulated, and remnants of compressed, relatively normal-appearing parathyroid tissue are seen at the edges. The cells of the tumor vary somewhat in size, have round vascular nuclei with sharp cell borders and clear cytoplasm. Occasional nuclei are large and somewhat hyperchromatic, but no mitoses are seen.

Diagnosis. Adenoma, benign, parathyroid gland, chief-cell type.

Jan. 14, 1955: Specimen. Adenoma, thyroid, right lobe.

Gross. Specimen consists of a rubbery firm mass of thyroid tissue measuring 3.0×2.7×1.3 cm. On section it has a uniform glistening colloid appearance, and multiple sectioning fails to reveal any recognizable parathyroid tissue. Most of the mass appears to be surrounded by a thin capsule.

Microscopic. Sections show encapsulated thyroid tissue composed of medium- to large-sized follicles well filled with colloid and lined by flattened epithelium. There are numerous areas of hemorrhage and scattered lymphoid infiltrations.

Diagnosis. Colloid adenoma, thyroid gland.

COMMENT

The four basic metabolic changes that occur with parathyroid hyperfunction are hyperphosphaturia, hypophosphatemia, hypercalcemia, and hypercalciuria.[11] At some stage in all cases of primary hyperparathyroidism these metabolic changes occur. However, marked renal insufficiency, if present, may becloud the issue by causing phosphorus retention, with a concomitant decrease in the serum calcium level. If prolonged, this may lead to parathyroid hyperplasia and eventually to secondary hyperparathyroidism.

There have been many theories advanced to explain the mechanism of the pathological changes in the acute intoxication of hyperparathyroidism. Hanes,[8] in 1939, in reporting the first instance of death in man due to acute parathyroid hormone poisoning, believed either that death resulted from myocardial failure due to severe myocardial lesions or that it had been a chemical death because phosphorus is not diffusible in the presence of a very high serum calcium level.

* Lt. Cmdr. M. S. Bowman (MC), U. S. N., provided the gross and microscopic descriptions.

Grollman,[12] in 1927, demonstrated that at high levels of serum calcium (about 18.0 mg. per 100 cc.) phosphate is no longer 100% filterable. Under these circumstances it was believed that precipitation of calcium occurred wherever there was localized tissue alkalinity. This was assumed to be the explanation of the deposition of calcium phosphate found in acid-secreting organs, such as the lungs, stomach, and kidneys. Shelling,[13] in 1938, presented another explanation in the nature of a chemical dysfunction. He believed that the most important factor in acute parthyroid intoxication was the marked diuresis accompanying parathyroid overactivity, resulting in dehydration and acute renal failure. Oliver,[1] in reporting two deaths from acute parathyroid crisis in 1939, postulated that death was due to a combination of dehydration and electrolyte loss plus a failure of the brain to utilize glucose in the absence of diffusible phosphorus. In effect, death was attributed to biochemical imbalance.

The terminal clinical picture in practically all of the reported cases has been one of oliguria, hyperpyrexia, cyanosis, coma, and circulatory collapse, a picture not unlike that seen in acute adrenal cortical insufficiency. In this day of the concept of the stress syndrome, this possibility might bear close scrutiny. It does not seem illogical to assume that chronic hyperparathyroidism and its associated profound metabolic alterations comprise an extremely potent situation of stress and that adrenal cortical insufficiency may develop.

The different theories offered to explain the cause of death in acute parathyroid intoxication suggest that the complete mechanism is not fully understood at the present time.

In every case of chronic hyperparathyroidism there is the potentiality of developing an acute parathyroid crisis. Fortunately, this complication is apparently rather uncommon. Whereas the causes of thyroid crisis are well known and quite apparent, the analogy does not carry over to explain parathyroid crisis. In 2 of the 14 cases of acute primary parathyroid intoxication reported in this series there is a definite record of ingestion of milk and absorbable alkali. In the two cases reported by Rogers,[6] acute parathyroid crisis apparently developed soon after the patient was placed on high calcium-absorbable alkali regimen in the treatment of duodenal ulcer. It was postulated that the resultant alkalosis produced precipitation of calcium in the renal tubules, resulting in acute renal failure and death.

An interesting factor in consideration of the causation of the acute symptoms concerns immobilization. It has been demonstrated that prolonged immobilization may produce skeletal demineralization with hypercalcemia and hypercalciuria. If this additive effect be superimposed upon a preexistent parathyroid hyperfunction, there could result an even greater degree of hypercalcemia and hypophosphatemia. The marked polyuria and renal tubular failure associated with chronic hyperparathyroidism would tend to produce excess chloride loss leading to a hypochloremic alkalosis. It has recently been shown that metabolic alkalosis may result in acute renal insufficiency.[14] This occurs most frequently in instances of antecedent renal disease but may occur in the absence of previous kidney disease. Thus it would appear that the additive hypercalcemic effect of skeletal disuse, the alkalosis, and the dehydration would favor renal tubular calcification, leading to further compromise of kidney function and conceivably an acute exacerbation of the hyperparathyroid state.

In the subject of this case report the acute symptoms began after the patient had been hospitalized for 15 days. The patient later reported that because of the pain in her lower extremities she got out of bed only to go to the bathroom. Thus, for all intents and purposes she was immobilized for practically all of this 15-day period. A perusal of the cases reported in this article discloses that in the great majority the patients had, in all probability, been bedridden for varying

intervals before the onset of the acute crisis. This observation would appear to lend support to the consideration that prolonged immobilization may well produce disastrous consequences in chronic hyperparathyroidism.

The clinical course and symptomatology reveal a strikingly similar picture in those cases of parathyroid crisis that have been reported. Before the onset of acute parathyroid intoxication, the patient usually presents symptoms of chronic hyperparathyroidism manifested by nausea, anorexia, constipation, weakness, polydipsia, and polyuria. The onset of parathyroid crisis would appear to be heralded clinically by the appearance of epigastric pain, vomiting, lethargy progressing to coma, oliguria, vasomotor instability, hyperpyrexia, and vascular collapse. A sudden elevation of the serum phosphorus and nonprotein nitrogen is a serious sign and may indicate impending parathyroid intoxication.[11]

In the particular case reported in this article it is difficult to evaluate the effect of the therapeutic measures instituted prior to surgery. The effect produced by the use of aqueous adrenal extract and hydrocortisone is practically impossible to assess in this isolated instance. It is believed that the energetic attempts at hydration with isotonic saline tended to minimize the hypochloremia and definitely improved the state of hydration. The recent use of the sympathomimetic amine levarterenol has added a potent therapeutic agent to the armamentarium in the treatment of shock. This patient received a continuous infusion of this drug prior to surgery and for about eight hours postoperatively. It is believed that this agent was in all probability the most important single factor in maintaining life until surgery was performed.

Another relatively new approach to the treatment of hypercalcemia, and conceivably to the treatment of parathyroid crisis, is the use of the disodium salt of the chelating agent edathamil (ethylenediaminetetraacetic acid; EDTA). Such compounds have found their widest range of usage to date in the treatment of lead poisoning; however, edathamil disodium has been found particularly effective in producing a transient but definite decrease in the serum calcium and in the dissolution of metastatic calcium deposits, particularly in the kidney. It would seem that this agent would be helpful in parathyroid crisis, especially in ameliorating the symptoms due to hypercalcemia per se, thus aiding in sustaining the patient until surgery can be performed. However, recent studies in the use of this drug in hypercalcemic conditions have shown that renal tubular damage and hemorrhagic manifestations may occur if large doses are used.[15]

Insofar as the surgical aspects of this disease are concerned, there are several important things to keep in mind. It is comforting to know that in approximately 80% to 85% of the cases of hyperparathyroidism the disease is due to a solitary adenoma. (In about 5% to 10% there may be more than one adenoma, and in another 10% there may be diffuse hyperplasia of all four parathyroid glands.) In the vast majority of cases the surgeon is searching for something considerably larger than the normal parathyroid gland, which has an average weight of only 35 mg. and is not always easily and quickly identifiable. In a series collected by Norris[16] from the literature, the average weight of the parathyroid adenoma was slightly in excess of 7 gm., although Black,[17] in reporting 80 cases from the Mayo Clinic, states that 50% of the adenomata were less than 1 gm. in weight, thus presenting a definite challenge to the surgeon who has to search for them. Most parathyroid adenoma will have a yellowish-brown or reddish-brown color and will display a definite capsule, with a more or less well-defined hilus through which delicate blood vessels enter. This characteristic color will usually serve to distinguish the tumor from lymph nodes, fat, thymus, or thyroid, but, if the surgeon is unsure, a frozen section will settle the question. In shape the adenoma will be oval or globular and it may have a flattened

appearance if compressed by neighboring structures.

Where should one begin the search for the offending adenoma? If a mass is present in the region of the thyroid gland which might be construed as arising from the parathyroid gland, the search should begin on that side. If there is no such clue, it makes no difference which lobe of the thyroid is mobilized first. The important features of the dissection are good exposure of the thyroid gland (best obtained by dividing and retracting the strap muscles), extensive mobilization of the lobes of the thyroid, and careful attention to hemostasis, since blood will stain parathyroid tissue and obscure its characteristic color. The most constant place to find the superior or true parathyroid (arising from the fourth branchial pouch) is, as has been pointed out by Lahey,[18] at the point where the recurrent laryngeal nerve passes under the lowermost fibers of the inferior constriction muscle as they attach to the horn of the thyroid cartilage. Here the parathyroid lies directly behind the upper pole of the thyroid gland at its junction with the middle third medially. It can best be demonstrated by ligating and severing the upper pole near the entrance of the superior thyroid vessels and then reflecting the distal portion of the gland downward and inward, where the parathyroid will be found at the point where the recurrent laryngeal nerve enters the larynx.

The inferior parathyroid (arising from the third branchial pouch) is most constantly found at the point where the inferior thyroid artery enters the posterolateral aspect of the body of the thyroid gland. It normally lies in a plane anterior to that of the superior parathyroid and is usually anterior to the recurrent laryngeal nerve and the inferior thyroid artery. However, it may be located almost anywhere about the lower pole of the thyroid gland.

Either parathyroid may have become displaced into the mediastinum. The superior gland, because of its posterior position, may descend into the posterior-superior mediastinum. The inferior gland may descend into either the anterior or the posterior mediastinum, depending upon its original position. In any event, the displaced gland carries its blood supply with it, and there is usually a definite vascular pedicle which may be traced from the inferior thyroid artery to the displaced gland. As stated by Black,[17] cervical adenomas of the parathyroid which have become displaced into the mediastinum are never deeply in the thorax and sternotomy will not be required for their removal. Only those very rare adenomas developing in parathyroids which were embryologically displaced well down into the anterior superior mediastinum would necessitate sternotomy. Also, in rare instances a parathyroid adenoma might be intrathyroidal.

Once having located and removed an adenoma of the parathyroid gland in a patient who is desperately ill from parathyroid crisis, it does not seem good surgical judgment to prolong the operation searching for other possible adenomata, since the chances of their being present are rather remote. This dictum, of course, does not hold true for the routine exploration of a patient suffering from chronic hyperparathyroidism without acute toxic manifestations.

On the other hand, if, as occurs in approximately 10% of cases of hyperparathyroidism, there is no adenoma but all of the parathyroid tissue is diffusely hypertrophied —primary or so-called wasserhelle hyperplasia—a subtotal resection of the parthyroid glands should certainly be considered.

Postoperatively a transient tetany may almost always be expected and is combated by intravenous calcium gluconate. In addition to the tetany, an oliguria will occur in the immediate postoperative period following excision of a hyperfunctioning parathyroid adenoma. This is due to a sudden decrease in circulating parathyroid hormone, with a resultant loss of its diuretic effect. The oliguria is the first clinical sign that the hyperparathyroidism has been cured. In cases where the hyperfunctioning tissue has not been removed, oliguria does not develop and intravenous fluids will be excreted almost quantitatively. Because oliguria favors

precipitation of calcium in the renal tubules and urinary tract, intravenous fluids should be given in the immediate postoperative period.

In the later postoperative period, treatment is in large measure dependent upon the presence or absence of bone involvement. If there has been no previous demineralization, the serum calcium and phosphorus may be expected to return to normal limits within several days. However, in those cases with osteitis fibrosa generalisata postoperative tetany is a problem. This problem is met by the use of a continuous intravenous infusion of calcium gluconate or lactate in the immediate postoperative course. In addition, it is necessary to maintain a satisfactory serum calcium level, even while replenishing the bones. Calcium is deposited in the bones as calcium phosphate. If the phosphorus intake is not limited, the bones are recalcified at the expense of the serum calcium. It is therefore necessary to restrict the dietary phosphorus postoperatively. This is accomplished by putting the patient on a high-calcium, low-phosphorus diet.[11] Vitamin D or dihydrotachysterol (AT 10) is administered to enhance calcium absorption from the gastrointestinal tract. In time the bones regain their calcium content with disappearance of the hypocalcemia.

SUMMARY AND CONCLUSIONS

The available literature on acute parathyroid crisis has been reviewed and another case reported, making 15 cases in all. The case reported in this paper was successfully treated by emergency parathyroidectomy.

Chronic hyperparathyroidism may undergo an acute exacerbation, with a high mortality rate. The onset of parathyroid crisis may be heralded clinically by the appearance of epigastric pain, vomiting, lethargy progressing to coma, oliguria, hyperpyrexia, and vascular collapse. A rising serum phosphorus and nonprotein nitrogen may indicate impending parathyroid intoxication.

The pathophysiologic mechanism producing the acute crisis is poorly understood. It appears that in several cases reported the use of a high calcium-absorbable alkali regimen had an adverse effect on the course of the disease. In addition, the presence of prolonged immobilization with skeletal demineralization may precipitate an acute crisis in a case of chronic hyperparathyroidism by aggravating a preexistent metabolic dysfunction. The possibility of adrenal cortical exhaustion from stress associated with chronic hyperparathyroidism is considered as a possible mechanism in the acute crisis of hyperparathyroidism.

In a suspected case of hyperparathyroidism under study it would appear advisable to maintain a low calcium intake, avoid undue immobilization, and correct serum electrolyte abnormalities promptly in order to avert dehydration and alkalosis. These factors enhance calcium precipitation in the renal tubules and may lead to acute renal insufficiency.

Surgical aspects of the disease have been considered, including the surgical approach as well as the pre- and postoperative care.

Acute primary hyperparathyroidism, or, more properly, an acute exacerbation or crisis occurring in a chronic primary hyperparathyroidism (due in most cases to a hyperfunctioning parathyroid adenoma), is a surgical emergency necessitating parathyroidectomy. As indicated in the review of the literature, failure to recognize the disease and failure to deal with it promptly when it was recognized resulted in an extremely high mortality rate in the cases reported.

Lt. Cmdr. R. W. Holmes (MC), U. S. N. rendered assistance in this study. Miss Melia R. Reed, medical librarian, helped in the preparation of the bibliographic references.

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Aortic Homograft Substitution for the Postrenal Inferior Vena Cava

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Although anomalies of the venous system are fairly frequent, those of the inferior vena cava are comparatively uncommon.

The human inferior vena cava is of complex origin (Fig. 1). It is derived from elements of nearly all the trunk veins of the embryo.[1] During the sixth, seventh, and eighth weeks of development, rapid changes take place in the mesonephros and the blood vessels associated with it. The postcardinal veins are the dorsal vessels of the mesonephros. They and the subcardinal veins, which lie ventromesially, are the dominant trunk vessels in the sixth week of development. The supracardinal veins which lie dorsomesial to the postcardinals develop rapidly during the seventh week. The posterior portion of the right supracardinal vein eventually becomes the postrenal vena cava of the adult. The left supracardinal vein largely disappears. By the end of the eighth week of intrauterine growth, the adult pattern has been established.[2]

The following case is one of agenesis of the postrenal portion of the inferior vena cava.

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From the Surgical Service of the Beekman Downtown Hospital.

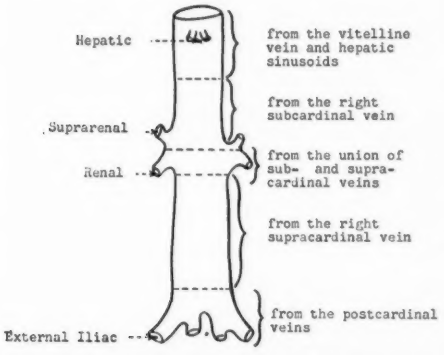


Fig. 1.—Anlagen of the human inferior vena cava (after Arey).

REPORT OF A CASE

A 29-year-old white married female decorator was admitted to the Beekman Downtown Hospital on May 31, 1954. Her chief complaint was one of recurrent, bilateral ankle ulcers of 12 years' duration. In addition, she suffered from extreme fatigue on long standing or other moderate physical exertion.

In her past history there was an episode of swelling of both legs associated with hematuria following a tonsillectomy in childhood. She was told that her kidneys were diseased, and her activities were limited for years thereafter. At the age of 17 years, a subcutaneous vein ruptured just above the right ankle. A year later the same thing happened in the left leg. When she was 19 years old a small ulcer formed over the right medial malleolus, and it persisted for one year. Roentgen irradiation was finally used. In the last four years there was a more or less constant persistence of ulceration about the ankles except for one period of several months of bed rest. As time went by the ulceration and resultant scarring became more bothersome, limiting her activity. Another complaint was one of menorrhagia, which had become very bothersome during the last three years and had not responded to two curettages.

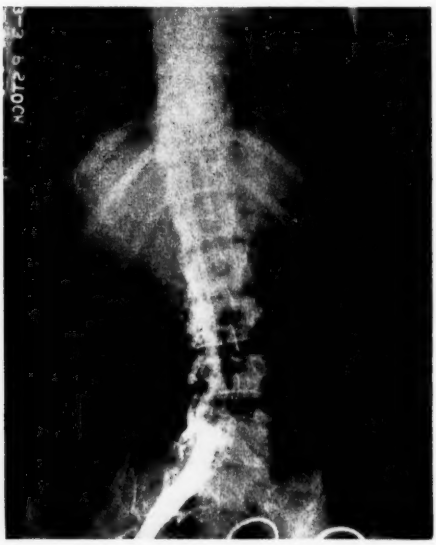
Physical examination revealed a well-developed and well-nourished young adult female. Huge, subcutaneous varices coursed through the integument of the trunk from both groins, over the abdomen, about the breasts, to the clavicles. These veins seemed to fill from below. There was an ulceration

1 cm. in diameter over the left medial malleolus, with considerable cellulitis about it. There were thin, circumscribed scars over both malleoli and lower legs. No evident varices were visible in the inferior extremities, except in the subinguinal regions. The contours and size of the inferior extremities were normal, as were the arterial vasculatures. The head was negative to physical examination, as was the neck. The lungs were clear both clinically and fluoroscopically. The heart was of normal size, with good quality sounds and no murmurs. The blood pressure, pulse, and temperature were normal. The abdomen was soft and nontender. There were no palpable masses. Vaginal and rectal examinations were negative.

All the laboratory data were negative, the blood count and urine being normal. The Wassermann test was negative. The prothrombin, bleeding, and clotting times were normal.

A venogram was obtained (Fig. 2) by the injection of 25 cc. of 35% iodopyracet (Diodrast) into the right femoral vein. This showed dilated right external and common iliac veins, with some opacity of the left common iliac vein. There was no shadow of an inferior vena cava. There were a few indistinct, small vessels above the confluence of the iliac veins. Intravenous pyelography suggested a normal kidney outline on the right; there was none on the left. Cystoscopy revealed only a small amount of urine of low specific gravity coming from the left ureter. It was believed that a contracted left kidney was present.

Fig. 2.—Preoperative venogram showing absence of inferior vena cava.



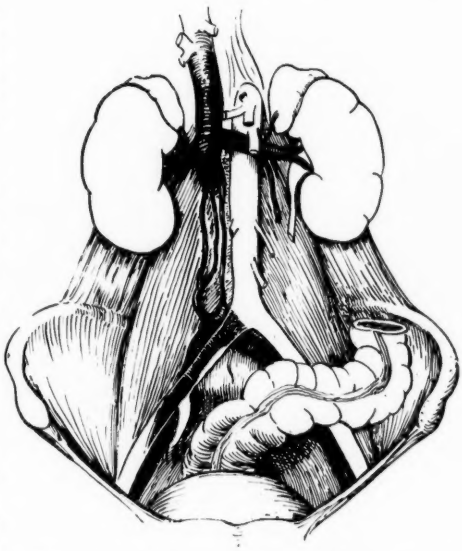


Fig. 3.—Findings at operation with agenesis of postrenal inferior vena cava.

Because of the history, physical findings, and roentgenograms, a diagnosis of obstruction of the inferior vena cava was made.

On June 2, 1954, laparotomy was performed through a paramedian incision extending from the ensiform cartilage to the pubis. Huge varices were found beneath the pelvic peritoneum. There was no free fluid. Both ovaries were markedly cystic. An incision was made in the parietal peritoneum just lateral to the ascending colon. The right colon, right kidney, and duodenum were then reflected medially with complete exposure of the right retroperitoneal space. There was no evidence of an inferior vena cava. From the confluence of the common iliac veins, three narrow venules, each 3 mm. in diameter, ran cephalad over the transverse processes of the third, fourth, and fifth lumbar vertebrae to end in a vein of 1.5 cm. diameter which then joined a small oblique right renal vein opposite the second lumbar vertebra. From this junction a vessel corresponding to the inferior vena cava in position, though smaller, continued upward (Fig. 3).

An aortic bifurcation homograft was then inserted, the cephalic anastomosis being located just below the junction with the right renal vein and the caudal anastomoses being made with the external iliac veins 4 cm. above the inguinal ligaments (Fig. 4). The left limb of the graft was placed beneath the root of the mesentery and the mesosigmoid. The graft filled promptly after release of the serrefines. Three rubber dam drains were

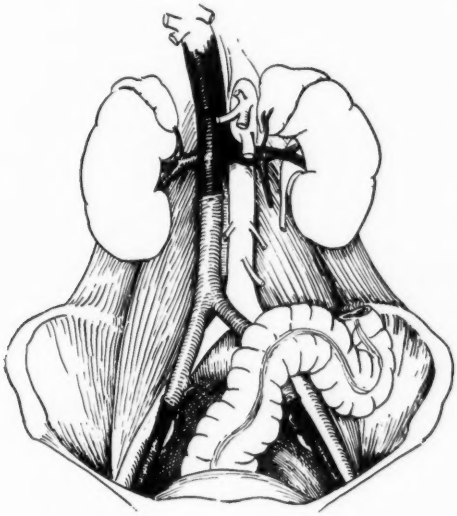
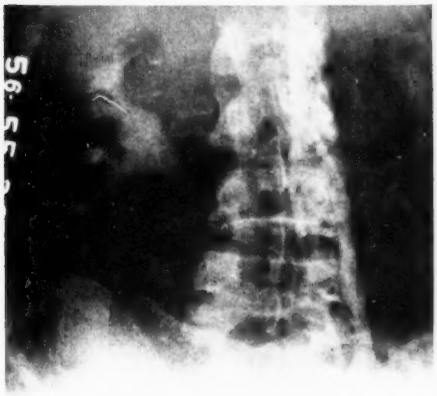


Fig. 4.—Aortic homograft in position.

placed in the pelvis and brought out through the inferior angle of the wound. The posterior parietal peritoneum was carefully closed over the entire extent of the graft. The wound was closed with interrupted figure-of-eight steel wire sutures including all layers except the skin. The skin edges were apposed with clips. Fine plastic catheters were inserted into both saphenous veins in order to provide a continuous postoperative heparin drip. This was allowed to run for 72 hours.

Fig. 5.—Venogram 11 months postoperative showing patent graft.



The patient withstood the prolonged procedure well. There was little postoperative reaction. She was allowed up in the third week and was discharged shortly thereafter.

She continued to do well. At four months, a check-up venogram with the contrast medium injected into the right femoral vein showed a patent graft. At 11 months, a venogram with introduction of iodopyracet into the left external iliac vein showed the graft to be patent, though somewhat pulled to the left (Fig. 5). During the 13 months since the operation, there has been no suggestion of an ulceration. The patient has led an active life, no longer finding it necessary to spend week ends in bed. Her job requires eight hours of walking about or standing each day, and her social activities at night have not been curtailed.

COMMENT

This is the first recorded case in which an aortic bifurcation homograft has been placed in the inferior vena cava. There are two cases in which a segment of aortic homograft has been placed in the superior vena cava. The first of these was a patient with mediastinal malignacy occluding the superior vena cava.[3] The graft was no longer patent four months after the procedure.* In the second superior vena cava case, the graft has remained patent 18 months up to the present.[4]

The problem of substitution in the venous tree is a more difficult one than on the arterial side. The low pressures and sluggish flow of blood increase the hazard of thrombosis. At the present time, even the plastic materials which are of great promise in arterial substitution have been found to be of questionable value in vein replacement.[5]

The fact that this patient is doing well one year after placement of the graft suggests that the best available material in situations of this kind is the arterial homograft whatever its method of preservation.

There is no mention in the literature of a congenital lesion resembling the one found in this case. However, we strongly believe that there was nothing in the appearance of the lesion to suggest obliterative thrombo-

* Holman, C. W.: Personal communication with the author.

phlebitis with cavernous reorganization. This latter lesion is well known to pathologists and is found at autopsy though unsuspected in life.

It is of significance that the supracardinal system, which gives rise to that portion of the inferior vena cava deficient in this particular instance, also provides the anlagen of azygous, hemiazygous, and lumbar veins. The poor collateral function resulting in the severe venous insufficiency of the lower half of the body can be readily explained by a congenital absence of these important components of the retroperitoneal venous system.

SUMMARY

A case of aortic bifurcation homograft substitution in the inferior vena cava is described.

The caval defect appeared to be a result of congenital deficiency of the supracardinal system of the embryo.

One year after the procedure the graft appears patent by venogram and the patient is symptom-free.

101 E. 93 St. (28) (Dr. Blum).

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Metabolic Derangements Imperiling the Perforated Ulcer Patient

VI. The Plan of Therapy

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INTRODUCTION

The mortality rate from perforation of peptic ulcers has been high and continues so unremittingly. In this hospital during the period from 1940 to 1952, one in every 11 patients admitted with a perforated ulcer succumbed.[1] This represents an appreciable improvement over the 44% mortality observed prior to 1916[2] and the 27% rate for the period between 1916 and 1940,[3] but in a surgical condition as common as this it seems unreasonable that so many cases should have had a fatal outcome. Comparable figures are reported from other hospitals.*

When the possible causes of the high mortality are examined, it becomes apparent that better management of the metabolic derangements associated with the condition should reduce the mortality more effectively than altering the type of operation. Good judgment in selecting the operative treatment to fit the mechanical problem involved in each case is not to be ignored, but we must not lose sight of the obvious fact that the number of fatalities is higher among patients treated by either gastrectomy or simple closure of their ulcers than among patients undergoing comparable operations without previous perforation. This fact emphasizes the significance of the perforation and consequent peritonitis and is a reminder that in the urgency to close the perforation there is insufficient time to repair any nutritional deficits of the preperforation illness. If therapy is to be improved, therefore, more attention should be given to the fluid, electrolyte, and nutritional management of the ulcer patient. As an example of what we mean, vigorous plasma therapy immediately after admission, with prompt restoration of the plasma volume, should do much to efface the time-honored rule that the longer the time between perforation and operation the higher the mortality.

The physiologic derangements and nutritional deficits imperiling the patient with a perforated peptic ulcer are described in the first five papers of this series. A plan of therapy based on these observations is presented here. The plan outlines general principles and indicates how details are to be modified to meet the requirements of the individual patient. Until a better method of caring for the metabolic derangements accompanying this disorder is established, we believe that the surgical approach is the treatment of choice and the operative procedure selected should be as simple as possible. The program of this paper assumes that simple closure of the ulcer will be employed.

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From the Department of Surgery, Harvard Medical School, and the Surgical Services, Massachusetts General Hospital.

* Mortality figures vary widely from hospital to hospital. In many instances this variation is due to differing policies in the selection of cases to be reported; references 4, 5, and 6.

PRINCIPLES OF THERAPY

The plan of therapy for the patient with a perforated peptic ulcer is best described in terms of phases and substances. In point of view of time there are five phases. The first three occur during the period of continued edema formation and are the preoperative, the intraoperative, and the immediate postoperative phases. The fourth is the subsequent phase of edema resorption, and the fifth is that of fluid equilibrium and resumption of intestinal function. The therapy must correct the deficiencies present on admission, buffer the additional burden of the operation, anticipate the continuing loss and subsequent resorption of fluid into the area of peritonitis, and, finally, satisfy the nutritional needs of the convalescence. These five phases are similar to those seen in burns.

The substances needed are of four types: water, colloids, electrolytes, and nutritional elements. These, too, are familiar from burn studies. Although each need is considered here in turn, in practice the four are interrelated and must be cared for simultaneously. At times provision for one may conflict with another. Adequate treatment of malnutrition, for example, is restrained, particularly in the edema-resorption phase, by fear of overhydration. The use of the renal output as the measure of the adequacy of fluid therapy is also described.

A. Fluid Volume Required.—The patient with a perforated peptic ulcer becomes dehydrated in six ways: seepage of fluid into the interstitial tissues of the peritoneum as edema, urinary excretion, gastric drainage, sweat, respiratory water loss, and, finally, blood loss at operation. From the standpoint of shock the most salient of these is the fluid lost from the plasma into the interstitial tissues. It determines largely the rate of fluid administration in the early hours.

The evidence available indicates that peritoneal edema is formed most rapidly in the initial hours, is formed more slowly for another day and a half, and is mainly resorbed in the subsequent two days. Direct measurements of this edema formation and resorption are not obtainable in the ulcer patient, but indirect evidence indicates that the edema shifts are similar to those in the patient with a cutaneous burn. Allusion has already been made to the resemblance between a burn and a chemical peritonitis following perforation.[7]

Uninfected partial thickness burns of the skin swell rapidly in the initial hours, reach their maximum swelling toward the end of the second 24 hours, and shrivel back nearly to normal size in the subsequent 48 hours. This clinical impression of the rate of edema formation and resorption in burns has been confirmed by objective volumetric measurements of burned hands.[8] Peak hand volumes are reached at about 36 to 48 hours after injury, and, in the absence of gross sepsis, most of the edema disappears in the next two days.[8] The process of resorption continues for several days before reaching completion. Diuresis, indicative of resorption, begins between the 30th and the 50th hour after the burn. In the ulcer patients evidence of initial hemoconcentration and subsequent hemodilution followed the same pattern and a mild diuresis was observed after the same interval following perforation trauma. Less conclusive evidence of the similarity of the fluid shifts in the two conditions is to be found in the changes of the thiocyanate and radioactive sodium spaces. The fallibility of these measurements is discussed in the third paper of this series.[9]

To keep pace with leakage of plasma fluid, the therapy must be intense in the early hours, slackening as interstitial tissue pressure increases and brings the further collection of edema to a halt. Once edema has reached its maximum, the need for this portion of the fluid therapy ceases. Prolongation of a high fluid intake into the period of edema resorption may burden the circulation and kidneys, but it is necessary to provide calories and nitrogen.

Fortunately, edema resorption, as indicated by diuresis, in the patients studied was a relatively minor event. The average increase in urinary output on the second

or third day in 17 cases was less than half a liter (Table 1), although the quantity of fluid administered averaged 3.2 liters on Days 2 and 3 and 3.4 liters on Day 1. Despite this rate of infusion, no clinical evidence of edema in undamaged tissues was observed.

Sufficient fluid for elimination of urinary waste products is easily provided if proper allowance has been made for other losses; a volume between 720 cc. and 1440 cc. of water in each 24 hours is theoretically adequate. In practice the need to carry in calories necessitates a larger intake than this and results in a greater urinary output than would be necessary were renal needs the only consideration.

Gastric fluid losses vary from patient to patient, generally being high at the outset and diminishing rapidly after the fourth postoperative day. In 17 patients of this series average losses on the day of perforation were 39 cc. per hour, the 24-hour totals ranging from 422 to 1513 cc. The subsequent daily losses are given in Table 1. Replacement of average volumes should be planned each day, and this replacement volume should be supplemented in any case in which gastric drainage exceeds half of the planned allowance of the first 12 hours.

In this study no attempt was made to measure the cutaneous and respiratory water losses of the ulcer patient. Crude calculations of the losses, based on their fluid balance and weight change data conform, however, to estimates of the losses based on more precise data in the literature (Appendix, Table A). We estimate that the patient with a perforated ulcer under "basal" conditions would have an insensible loss of 1.6 kg. on the day after perforation, 1.4 kg., 1.2 kg., and 1.0 kg., on the three succeeding days, and about 0.8 kg. a day thereafter. The basis for these calculations is given in the Appendix. Actual losses would be slightly higher. We suggest replacement of 1.75 liters for the day of perforation and the two succeeding days and 1 to 1.5 liters thereafter. A small portion (0.2 to 0.3 liters) of this loss will be met by the water of metabolism.[10]

Both blood and tissue fluid are lost during operation. The blood loss was not measured in this series, but the literature records losses of between 15 cc. and 150 cc. for comparable operations (Appendix II, Table B). In our own experience with measurement of blood loss during operation, the actuality tends to exceed the estimate. Routine administration of 250 cc. is recommended in the plan to assure coverage of this loss. More is to be given in cases suspected of a preexisting anemia, that is, those patients without an elevated hematocrit reading on admission.

Tissue fluid losses at operation in four cases averaged 193 cc. (38 cc. to 410 cc.). Replacement is achieved by increasing the hourly infusion of electrolyte solution during the procedure.

B. Colloid Requirement. — A colloid is needed to replenish the plasma proteins because proteins are lost along with the water seeping out of the vascular bed into the area of peritonitis.

The concentration of the colloid to be given must be estimated indirectly. The protein concentration in the free peritoneal fluid of the patients studied was 4.6 gm/100 cc., but dilution by fluid escaping through the perforation or by peptic digestion may have altered the protein concentration. It corresponds closely, however, to the 4.5 gm/100 cc. concentration found in the bleb fluid of cutaneous burns.[11] Another similarity between the burned patient and the patient with a perforated ulcer also suggests that the 4.6 gm. concentration may be close to that of the edema fluid, namely, the early rise in protein concentration of the residual circulating plasma in the untreated patient. In the burned patient proportionately less plasma protein than water seeps out of the capillaries. The protein retained increases the protein concentration of the residual circulating plasma. The initially high protein concentration of the ulcer patient indicates a comparable propor-

TABLE 1.—*Fluid, Electrolyte, and Nitrogen Outputs of the Average Patient with a Perforated Ulcer Treated by Surgical Closure*

Post-operative Day	Fluid Output (17 Cases)				Potassium Output (14 Cases)				Phosphorus Output (12 Cases)				Sodium Output (14 Cases)				Chloride Output (12 Cases)				Nitrogen Output (16 Cases)			
	Urine, Cc.	Stool, Cc.	Gastric Fluid, Cc.	Total, Cc.	Urine, Gm.	Stool, Gm.	Gastric Fluid, Gm.	Total, Gm.	Urine, Gm.	Stool, Gm.	Gastric Fluid, Gm.	Total, Gm.	Urine, Gm.	Stool, Gm.	Gastric Fluid, Gm.	Total, Gm.	Urine, Gm.	Stool, Gm.	Gastric Fluid, Gm.	Total, Gm.	Urine, Gm.	Stool, Gm.	Gastric Fluid, Gm.	Total, Gm.
0*	753	0	435	1,188	1.7	0	0.1	1.8	0.5	0	0.2	0.7	1.2	0	0.6	1.8	1.4	0	1.2	2.6	4.8	0	1.4	6.2
1	1,368	0	618	1,986	2.3	0	0.2	2.5	0.8	0	0.3	1.1	2.4	0	1.0	3.4	3.0	0	1.7	4.7	10.7	0	0.8	11.5
2	1,673	0	643	2,316	2.2	0	0.3	2.5	0.7	0	0.1	0.8	2.6	0	1.0	3.6	3.3	0	2.3	5.6	13.6	0	0.9	14.5
3	1,440	†	686	2,126	1.6	0	0.3	1.9	0.5	0	0.1	0.6	2.7	0	1.1	3.8	2.7	0	3.5	6.2	13.1	0.2	0.7	14.0
4	1,468	†	441	1,909	1.5	0.1	0	1.6	0.5	0	0	0.5	2.5	0.1	0.5	3.1	3.3	0.1	1.9	5.3	13.7	0.5	0.3	14.5
5	1,651	†	183	1,834	1.2	0	0	1.2	0.4	0.1	0	0.5	2.5	0.1	0.2	2.8	2.2	0.1	0.8	3.1	11.9	0.4	0.2	12.5
6	1,468	†	124	1,592	1.4	0.3	0.1	1.8	0.5	0.5	0	1.0	2.5	0.3	0.3	3.1	2.5	0.2	1.0	3.7	11.8	1.0	0.2	13.0
7	1,330	†	27	1,357	1.2	0.2	0	1.4	0.7	0.2	0	0.9	2.0	0.2	0.1	2.3	2.0	0.1	0.2	2.3	11.4	1.2	0	12.6
8	1,402	†	0	1,402	1.5	0.4	0	1.9	0.6	0.3	0	0.9	2.2	0.2	0	2.4	2.3	0.1	0	2.4	12.3	1.5	0	13.8

* The start of a balance day was 9 a. m. The length of Day 0 varied according to the time at which the patients entered the hospital. The average duration of Day 0 for the 17 patients whose fluid outputs were measured was 11.1 hr. The average duration of Day 0 in the cases whose K + Na outputs were measured was 9 hr., P + Cl outputs 11 hr., and N output 12 hr.

† Water loss through the stools was not measured.

tionate loss. In the fluid therapy of the ulcer patient, therefore, it is recommended that the colloid solution given to replace this portion of the fluid lost be the equivalent of 4.5 gm/100 cc. of plasma protein.

The colloid of preference is human plasma protein. These proteins are nonantigenic and are metabolized, providing nitrogen and calories. Other colloids may be used if plasma is not available.† Dilution of blood-bank plasma with a protein-free electrolyte solution to form an 80% plasma-20% electrolyte mixture generally will reduce the protein concentration to the desired 4.5 gm/100 cc.‡ In cases with preexisting anemia or extensive blood loss, some of the plasma should be replaced by whole blood. The practice of substituting blood for all of the plasma needed is to be avoided, since this raises the hematocrit level and viscosity of the circulating blood above normal.[13]

The volume of the colloid solution required is moderate and probably less than would be needed if the therapy were composed solely of noncolloidal solutions. Electrolytes and water, when given intravenously, distribute themselves rapidly and evenly throughout the entire extracellular fluid. Colloids, on the other hand, permeate slowly, except in the damaged areas, and, retained within the blood stream, they maintain plasma volume.

The final argument in favor of the use of a colloidal solution is that, in reducing the volume needed, an unnecessary excess of water and electrolytes is averted. The eventual problem of excretion of these excesses is reduced.

In practice the volume of colloid-electrolyte mixture needed is 1.2 liters. This was found to be the average volume of edema in the patients studied (Paper III).[9] This edema volume is comparable to that of a 10% to 15% body surface burn in an adult. With the assumption that in patients with perforated ulcers, as in those with burns,[14] half of the edema formation takes place in the first eight hours, a minimum allowance of 600 cc. of fluid must be made in the first eight hours to compensate for edema formation. Allowance of 700 cc., as outlined in the plan here, may be wiser, since correction of hypotension will inevitably increase capillary filtration pressure and, hence, plasma loss.

C. Electrolyte Needs.—Recovery of the patient with a perforated peptic ulcer may also depend on selective management of the electrolyte intake. The plan of therapy must control the amounts of potassium and sodium. Phosphorus and chloride are also given. From the findings reported in Papers II through IV of this series, control of potassium would seem to be the most important.§ Unless potassium is supplied as the normal water volume is rebuilt, the serum potassium concentration will drop below normal. Hypopotassemia is an undesirable and avoidable complication. During the first 48 hours after perforation, potassium is excreted in excess through the kidneys (Table 3, Paper II[15]). Smaller amounts are lost through gastric drainage, sweat, and, later, the stools. The greatest amount of potassium was lost by the patients of this series in the first two days (daily average 75 mEq., or 2.9 gm.). Subsequent daily outputs were smaller (Table 1). Since much of the infused potassium is excreted, a greater amount is required to achieve balance or potassium retention. We have been successful in maintaining positive balance, except on the day of perforation, by administration of 75 mEq. (2.9 gm.) of potassium a day.[13]

† The use of plasma which has not been pooled and which has been stored in a liquid state at room temperature for six months is routine in this hospital. Allen and co-workers have found that storage of pooled plasma in this manner reduces the risk of homologous serum jaundice almost to zero.[12] Use of unpooled plasma may decrease the statistical chance of jaundice still further.

‡ In a few hospitals 25 cc. of 50% dextrose is now being added to citrated plasma to prevent late fibrin formation. In our experience the resulting plasma protein concentration averages 5.2 gm. A slightly higher percentage of plasma in the plasma-electrolyte mixture is in order when this practice is followed.

§ References 9, 15, and 16.

The fluid used to make good the plasma losses into the interstitial tissues of the peritoneum should contain sodium. The sodium needed constitutes yet another advantage of selecting plasma for colloid replacement, since plasma contains sodium in the desired concentration. If a salt-free colloid is used, supplementary sodium should be given. Very little additional sodium is needed by the ulcer patient. Enough should be given to replace the renal, sweat, and gastric sodium outputs, but no attempt should be made to "treat" the chemical findings. The drops in serum chloride and sodium concentrations do not represent salt depletion and should cause no apprehension. Similar drops are seen during edema formation in burns, and the low levels stubbornly resist attempts at correction by saline infusion. Vigorous saline therapy is of little, if any, benefit in either condition and may exaggerate the edema formation. Less sodium is needed in the ulcer patient than in the patient with an equivalent burn, because there is no external loss of sodium comparable to that in the burn exudate.‖

As parenteral feeding gives way to oral feeding at the end of the first week after perforation, administration of a nearly sodium-free diet leads to a cumulative sodium deficit.[9] No ill effects of this deficit were observed in the study, but it is probably wise to provide a moderate amount of sodium with the bland diet to prevent sodium depletion.

Chloride therapy, as far as we know, does not present a separate problem. Historically, chloride was the first electrolyte to receive the attention of the surgeon. This was because its concentrations were so easy to determine chemically. Now that sodium concentrations are readily measured, following the chloride levels is no longer as informative as following the base levels. In general, chloride shifts with the sodium, although it is lost in excess of base through gastric drainage if the stomach is actively secreting. Serum chloride concentrations vary widely in the ulcer patient, but the variations are compensated for by CO_2. In the patients studied no ill effects were ascribed to the wide shifts observed. In practice the chloride needs no special attention if the needed sodium is given as the chloride.

Although no need for phosphorus has been proved in the ulcer patient, phosphorus is an important tissue component and its administration is recommended in the plan. Following perforation there is a urinary outpouring of phosphorus similar to, but less intense and less prolonged than, that of potassium.[15] Compensation for this loss is easily accomplished by phosphorus administration. Other losses of phosphorus are minor.

To supply the major portion of these needed electrolytes, we recommend a multiple electrolyte solution first described by Talbot, Crawford, and Butler.[17] The composition of this solution is given in Table 2. The solution provides the following electrolytes:

TABLE 2.—*Multiple Electrolyte Solution* *

Anhydrous dibasic potassium phosphate	24.4 gm.
Monobasic potassium phosphate	4.0 gm.
Anhydrous sodium lactate	44.8 gm.
Potassium chloride	30.0 gm.
Sodium chloride	23.4 gm.
Dextrose	50 or 100.0 gm.
Distilled water	q.s. ad 1000.0 cc.

* This solution is commercially available.

Electrolyte	mEq. per Liter
Sodium	40.0
Potassium	35.5
Chloride	40.0
Lactate	20.0
Phosphate	15.5

In addition, the solution provides 500 cc. of free water per liter for renal and respiratory needs. The osmolar concentration after the dextrose is metabolized is only 151 mOsm., as compared with nearly 300 in isotonic saline or in human extracellular fluid. There is no need to fear potassium intoxication from this potassium solution. It is of low concentration and is immediately diluted by diffusion throughout the extracellular fluid space.

‖ Cope, O., and Minor, C. L., unpublished data.

Whether or not there is a need following perforation for magnesium, calcium, or other electrolytes has not been shown. The answer awaits further study.

D. Nutritional Needs.—The nutritional needs of the patient with a perforated peptic ulcer are greater than those of the normal person undergoing a comparable operation. The patient is generally malnourished prior to perforation ¶ and has an elevated metabolic rate for the first few days after perforation (Table, Paper V [18]). In addition, the patient theoretically may suffer from a subclinical vitamin deficiency due to prolonged dietary restrictions. Unfortunately, ideal nutritional therapy is not possible during the early postoperative period, because the perforation and peritonitis prevent normal gastric and intestinal function, rendering the oral route of nourishment useless. The intravenous route can be used beneficially to administer many nutriments, but volume limitations make it difficult and often impossible to maintain the total nutrition, even of a resting patient. Fat preparations are not yet sufficiently free of reactions to justify recommendation of their routine use. In the critically ill, sorely undernourished patient, however, these preparations may be lifesaving. In this hospital a little less than 10% of patients receiving fat infusions react with fever.[19]

Dependence is placed, therefore, upon carbohydrates and nitrogen. Except during the preoperative and operative phases, we recommend that 10% dextrose be used in preference to the isotonic 5%. We incline to avoid the more hypertonic carbohydrate in the initial hours for two reasons: to avert unnecessary urinary excretion and to avert further dehydration of uninjured tissues. After operation we advocate 10% dextrose to increase the caloric intake.

Nitrogen depletion after perforation has been shown in this study to be a preventable complication and one which can be remedied by intravenous administration of an adequate quantity of amino acid hydrolysates.[14] The nitrogen depletion results from nitrogen lack rather than excessive nitrogen elimination. When the nitrogen is administered intravenously in the form of amino acids, urinary nitrogen excretion increases sharply; however, if enough nitrogen is given, appreciable amounts are retained. Intakes of approximately 20 gm. daily are recommended to minimize or prevent a nitrogen depletion in the first week after perforation. By the ninth day 10 gm. is generally adequate, but higher intakes will result in greater nitrogen retention.

Regarding vitamins, no study was made. We assume that it is wise to supply them to cover any preexisting deficiency or special need.

E. Use of the Urinary Output as an Estimate of Plasma Replenishment.—Urinary excretion, in our experience, is the most prompt and sensitive indicator of the adequacy of fluid therapy during edema formation in the ulcer patient. If therapy fails to keep pace with the plasma loss, renal blood flow diminishes, glomerular filtration dwindles, and the urinary output falls. With improvement in the plasma volume, filtration and output increase. The flow of urine indicates, therefore, the adequacy of the plasma volume. It proved a valuable measure of hydration in the burned patient and was, therefore, adapted to the ulcer patient. It has been our practice to put in an indwelling catheter on admission.#

The first 36 hours after perforation are the troublous time. Intravenous fluid infusion should be started as soon as the diagnosis of a perforation is made and should be continued throughout the whole stage of edema formation, for shock is impending as long as plasma is being lost from the circulation.

Operation is not to be undertaken until the plasma volume has been brought to normal, as indicated by an hourly urine

¶ References 7 and 16.

Spontaneous voiding does not permit a sufficiently accurate check on the fluid needs and may be grossly misleading if any degree of postoperative atony of the bladder develops.

output greater than 20 cc. This precaution before operation is necessary, since the vascular bed may enlarge considerably during anesthesia. Failure to restore the plasma volume preoperatively invites shock. If the hematocrit level is measured after urinary excretion becomes adequate, it will be found to have returned to the normal range.

THE PLAN

The Preoperative Phase.—Elimination of Deficiencies Present on Admission: An hour, or an hour and a half, should suffice for restoration of the plasma volume and renal plasma flow. A greater time may obviously be necessary with a patient who has had a long interval between perforation and arrival at the hospital.

TABLE 3.—*Guide to Parenteral Therapy for the Preoperative Phase Arranged According to Time of Admission After Perforation and to be Modified According to Renal Output*

Hours Between Perforation and Admission	Plasma, Cc.	5% Dextrose in Saline, Cc.	5% Dextrose in Water, Cc.	Multiple Electrolyte Solution, Cc.	Total, Cc.
0	100	100	100	0	300
1	200	200	200	0	600
2	300	300	300	0	900
3	400	400	400	0	1,200
4	450	325	325	250	1,350
5	500	375	375	250	1,500
6	550	425	425	250	1,650
7	575	475	475	250	1,775
8	600	650	500	250	2,000
9	625	700	550	250	2,125
10	650	750	600	250	2,250
11	675	800	650	250	2,375
12	700	850	600	500	2,650

The amount of fluid needed to resolve the plasma volume and rehydrate the patient is not an absolute one. The volumes suggested below and in Table 3 are to be used in planning. They are to be modified according to the urinary output and the laboratory measurements.

For patients whose ulcers have been perforated for two hours, we suggest that the initial plan be 300 cc. each of plasma, 5% dextrose in saline, and 5% dextrose in water. This quantity should provide the needed water and electrolytes for external losses and leave enough for edema formation. For patients admitted three hours after perforation the planned mixture should contain 400 cc. of each (300 drops a minute). If one intravenous set-up is inadequate to deliver this volume, two should be used. The rapid infusion should be continued into the second hour, if a satisfactory urinary output does not result.

The fluid recommendations for longer intervals are given in Table 3. It will be seen that the plan calls for smaller increases in the plasma than in the water and saline as edema formation slows.

Some of the potassium and phosphorus lost from the body in this phase will be replaced by the ions present in the plasma. If perforation has occurred within four hours of the time of entry, the dehydration will be relatively moderate and the infusion of potassium and phosphorus may be postponed until after the operation. In patients with perforations four hours old or older, an infusion of multiple electrolyte solution should be started as soon as renal function is assured (Table 3).

The Operative Phase.—When urinary flow is reestablished, operation can be undertaken. During the procedure the following fluids are given to meet the new and continuing losses: 250 cc. of whole blood and 100 cc. each of plasma, 5% dextrose in saline, and 5% dextrose in water. If the operation takes more than an hour, these volumes are to be repeated hourly. More blood is to be supplied if blood loss exceeds 250 cc. The indwelling catheter should be connected to a small bottle during the operation and the hourly output calculated at the end of the procedure to aid in determining whether the subsequent plan of therapy should be modified.

The Postoperative Phase of Continuing Edema Formation.—The quantity of fluid needed postoperatively depends upon the urinary response and upon the time at which the operation is completed. In this

phase, as in the preceding and succeeding ones, the basic plan is modified according to the renal output. The gastric output should be totaled at the 12th hour and the allowance of saline increased if the loss exceeds 450 cc.

At the end of the eighth hour after perforation, half of the fluid planned for replenishment of edema losses (700 cc. of diluted plasma) should have been infused in addition to the amount needed to keep pace with external losses.

The recommended postoperative allowance for the remainder of the first eight hours after perforation are as follows:

10% dextrose in saline	70 cc/hr.
10% dextrose in water	60 cc/hr.
Plasma	40 cc/hr.
Multiple electrolyte solution in 10% dextrose	30 cc/hr.

For the 8th through the 24th hour after perforation the following allowances are recommended:

Plasma (20 cc/hr.)	320 cc.
Multiple electrolyte solution in 10% dextrose (150 cc/hr.)	2,400 cc.
Total	2,720 cc.

This allowance supplies adequate fluid: 25 cc. of fluid per hour for edema formation (protein concentration 4.5 gm/100 cc.), 30 cc. for gastric loss, 65 cc. for sweat and insensible loss, and 50 cc. for urinary excretion. Free water is available from the multiple electrolyte solution when the dextrose is metabolized. For patients admitted within 12 hours after perforation, these solutions in combination with those recommended for the preoperative and operative phases provide the requisite electrolytes for the first 24 hours, namely, 96-77 mEq. of potassium,* 1.3-1.0 gm. of phosphorus, 320-361 mEq. of sodium, and 274-320 mEq. of chloride. Nitrogen and caloric requirements are partially met: 8.5 to 11.2 gm. of nitrogen and 1425 to 950 calories are included (Tables 4 and 5). Indicated antibiotics and vitamins may be given separately or, if suitable for intravenous use, in the mutiple electrolyte solution.

For the final 12 hours of the edema formation phase, plasma replacement may be continued at the same rate, but the addition of an amino-acid hydrolysate solution containing both nitrogen and electrolytes will permit a reduction in the volume of multiple electrolyte solution. The amino acids should be started as soon as the plasma infusion is completed †; 500 cc. of 10% amino-acid hydrolysate in 5% dextrose is recommended.

TABLE 4.—*Estimated Electrolyte Requirements for First Twenty-Four Hours* *

	K (mEq.)	P (Mg.)	Na (mEq.)	Cl (mEq.)
To replace electrolytes displaced in edema water	4.5	3	127	93
For gastric loss	6	330	52	62
For cutaneous loss	2-4	4-15	17-85	17-85
For urinary loss	77	960	113	87
	89.5-91.5	1297-1308	309-377	259-327

* Exclusive of electrolytes in whole blood loss, replaced quantitatively by whole blood transfusion.

* The initial figure given for each electrolyte is the amount supplied if the patient is admitted one hour after perforation and the second figure the amount supplied if admission is delayed until the 12th hour.

† The manufacturers of many hydrolysate preparations recommend that, if plasma or whole blood has been given, the tubing should be changed before starting the hydrolysate infusion.

TABLE 5.—*Electrolyte Composition of Parenterally Administered Solutions*

Solution	Potassium		Phosphorus,	Sodium		Chloride	
	Mg/100 Cc.	mEq/L.	Mg/100 Cc.	Mg/100 Cc.	mEq/L.	Mg/100 Cc.	mEq/L.
K-B solution	1,498	38.3	178	1,374	59.7	1,678	47.3
10% Protein hydrolysate injection (amigen)	30	0.8	90	150	6.5	200	5.6
Whole blood (85 cc.) plus preservative (15 cc.)	192	4.9	3	211	9.2	247	7.0
"Normal" saline (0.85%)	0	0	0	335	14.6	515	14.5
Plasma	20	0.5	3	327	14.2	365	10.3
Multiple electrolyte solution	138.8	3.5	48	92	4.0	142	4.0

The plan for the first half of the first postoperative day (24th-36th hr.) is as follows:

Plasma	240 cc.
Multiple electrolyte solution in 10% dextrose	1,500 cc.
10% amino-acid hydrolysate in 5% dextrose	500 cc.
Total	2,240 cc.

The Phase of Edema Resorption.—Because of nutritional needs the plan of fluid therapy for this phase is not restrained, but the patient should be watched to be sure that signs of overhydration do not develop. The proposed intake should be cut back if urinary output exceeds 75 cc. per hour. To provide the nitrogen recommended and fill the major part of the day's caloric requirements, *the plan for the remainder of the first postoperative day (36th-48th hr.) calls for the following:*

5% amino-acid hydrolysate in 10% dextrose	2,000 cc.

These allowances for the first postoperative day supply 66 mEq. of potassium, 2.1 gm. of phosphorus, 192 mEq. of sodium, 169 mEq. of chloride, 20.9 gm. of nitrogen, and 2022 calories. The therapy is not ideal from the caloric standpoint, but it approximates the estimated requirements fairly well in view of the limitations on fluid volume. Sodium and chloride replacement in this phase is low, since the edema fluid returning to the circulation is rich in extracellular electrolytes. On this and all subsequent days vitamins should be given.

The following solutions are suggested for the second and third postoperative days:

10% amino-acid hydrolysate in 5% dextrose	1,000 cc.
5% amino-acid hydrolysate in 10% dextrose	1,500 cc.
Multiple electrolyte solution in 10% dextrose	1,500 cc.
Daily total	4,000 cc.

These quantities will supply the patient with 1925 calories, 21 gm. of nitrogen, 68 mEq. of potassium, 2.3 gm. of phosphorus, 175 mEq. of sodium, and 158 mEq. of chloride. The fluid volume may prove excessive. The renal output should, therefore, be carefully followed.

The Postresorption Phase.—This phase marks the end of the period of mandatory intestinal rest and the beginning of a gradually increasing schedule of oral feedings. Restoration of the oral alimentation should proceed as rapidly as the individual patient is able to tolerate it, rather than according to a set plan. The practice which proved satisfactory in the patients of this study was to clamp the nasogastric tube off on the fourth postoperative day, aspirating the gastric contents hourly. After each aspiration the patient was permitted 30 cc. of water by mouth. If the gastric residuum at the end of an hour was small, the quantity given was increased. Milk was substituted as soon as 60 cc. of water an hour was tolerated. The nasogastric tube was clamped for longer intervals when it became evident that the stomach was emptying satisfactorily. It was removed altogether when gastric retention was absent or minimal after clamping for a six- to eight-hour period. On the fifth postoperative day the majority of the patients were taking 60 cc. of milk an hour, and on the following day the allowance was usually changed to 120 cc. every two hours. By the seventh and eighth days the quantity tolerated was generally between 180 and 240 cc. every three hours, and some patients were tolerating soft bland foods.

Until oral feedings are well reestablished, nutritional supplements should be given by vein. The inclination to omit parenteral feedings as soon as the patient is taking small amounts by mouth is best resisted. Milk given on the fourth and fifth days will rarely provide more than 100 and 700 calories, respectively. We suggest the following *fluids for the fourth, fifth and sixth postoperative days:*

5% amino-acid hydrolysate in 10% dextrose	2,000 cc.
Multiple electrolyte solution in 10% dextrose	1,000 cc.
Daily total (exclusive of oral feedings)	3,000 cc.

On the seventh postoperative day 2000 cc. of 5% amino-acid hydrolysate solution in 10% dextrose will probably be needed, unless the patient manages to take more than 1600 cc. of milk. That amount, together with the amino-acid solution, will supply sufficient electrolytes to make additional electrolyte infusions unnecessary. On sub-

sequent days the quantity of the amino-acid solution can be further decreased.

As soon as the patient is receiving exclusively oral alimentation, some sodium chloride should be included in the diet.

SUMMARY

A plan of therapy for the patient with a perforated ulcer is presented. The plan is based on observations of the metabolic and nutritional derangements in 24 patients experiencing ulcer perforation. The importance of early vigorous preoperative plasma therapy and adequate replacement of lost potassium and nitrogen is emphasized. The adequacy of the fluid therapy in the shock phase is best judged by the renal output.

APPENDIX

I. Insensible Water Loss

Insensible water loss from the lungs and skin of the patients in this series has been estimated from their metabolic rates. Benedict and Root [20] have demonstrated that insensible loss bears nearly a straight-line relationship to heat production. Their curve was used in calculating the estimated losses in Table A. Crude figures are also given for the observed water losses. These figures are based on the sum of the observed weight loss and the positive fluid balance, given in kilograms. No correction has been made for nonfluid weight loss (tissue or CO_2) or for oxygen absorption. Where weight gains were observed no figures are given. The estimated figures conform well with the observed losses if a daily tissue weight loss of 0.3 gm. is assumed.

Table A

Day After Perforation and Operation	Average Heat Production Under Resting Conditions (Calories per 24 Hr.)	Estimated Insensible Water Loss (Resting) (Kg/Day)	Observed Insensible Water Loss	
			Patients, No.	(Kg/Day)
1	2,597	1.6*	..	†
2	2,227	1.4	7	1.7
3	2,167	1.2	8	1.7
4	1,807	1.0	10	1.3
5	1,637	0.9	8	1.4
6	1,495	0.8	7	1.6
7	1,535	0.8	8	1.2
8	1,408	0.7	..	...
9	1,404	0.7	..	...

* This figure based on extrapolation of the curve of Benedict and Root.
† Weight gain.

II. Operative Blood Loss

Table B

(Data from the Literature)

Operation	Cases, No.	Operative Blood Loss: Maximum, Cc.	Minimum, Cc.	Average, Cc.
Abdominal laparotomy [21]	1	..	..	120
Appendectomy [21]	6	8	4	6
Appendectomy and repair [21]	1	..	..	62
Appendectomy and uterine suspension [21]	3	28	17	22
Cholecystectomy [21]	3	145	51	87
Hernioplasty [21]	1	..	..	32
Appendectomy [22]	2	14	13	13
Appendectomy and hernioplasty [22]	1	..	..	54
Cholecystectomy [22]	1	..	..	55
Hernioplasty [22]	2	51	13	32
Appendectomy and uterine suspension [23]	1	..	..	96
Colporrhaphy and laparotomy [23]	1	..	..	297
Gastric resection [23]	1	..	..	256
Hernioplasty [23]	1	..	..	79
Pelvic laparotomy [23]	1	..	..	162
Appendectomy [24]	16	124	8	51
Gastrectomy [24]	18	1640	349	855
Gastro-enterostomy [24]	1	..	..	109
Gastrostomy [24]	3	78	38	54
Hernioplasty [24]	20	212	25	73

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Surgical Experiences in Portal Hypertension

A Review of Nineteen Cases from Brooke Army Hospital

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INTRODUCTION

The literature dealing with surgical aspects of portal hypertension in the past few years has been voluminous, and the ideas expressed have been sufficiently divergent that some doubt has arisen as to the validity of the feeling that portacaval anastomosis is beneficial and worth while. Our work in this complicated field has been predicated on the philosophy that cirrhosis of the liver or some other cause of portal hypertension is outside the scope of surgical attack and that our narrow sphere of usefulness to the patient lies in prevention of death from esophageal varix hemorrhage secondary to the obstruction to portal flow. Thus, our approach is a mechanical one, based on an attempt to reduce portal pressure to the point where esophageal varices disappear or have such a reduced pressure that they are unlikely to erode or rupture and bleed. We therefore have put great emphasis on pre- and postoperative pressure readings in these varices. All of the pressure readings in our patients have been made through the esophagoscope by Col. Benjamin Sullivan (MC), formerly Chief of Gastroenterology at Brooke Army Hospital and now holding the same title at Letterman Army Hospital. We are indebted to him for the careful work-up of our patients. From August, 1952, through July, 1954, there have been 19 patients subjected to surgery for portal hypertension at Brooke Army Hospital, and these cases form the background for our discussion. All of the shunts have been done by one of us (W. F. B.), although the remainder of the work has been a joint effort.

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ETIOLOGY OF PORTAL SYSTEM BLOCK

The original concept of portal-bed block is generally attributed to Banti. Marked impetus to interest in this field followed reports in 1934 by Larrabee,[1] in Boston, and in 1936 by Rousselot,[2] in New York, when they independently incriminated the liver as being the site of obstruction in the portal system. Since that time, it has become recognized through the classical dog studies of Whipple and others that portal hypertension can exist on the basis of a block in the liver itself or in the portal system vessels outside the liver. Foster's[3] classification of the causes of portal hypertension are listed below:

A. Intrahepatic block
   1. Laennec's cirrhosis
   2. Postnecrotic cirrhosis
      a. Infectious
      b. Toxic
   3. Biliary cirrhosis
   4. Syphilitic liver disease
   5. Schistosomiasis

B. Extrahepatic block
   1. Venous
      a. Thrombosis of portal or splenic veins due to trauma, infection, stasis due to intrahepatic obstruction, or spontaneous thrombosis
      b. Developmental constrictive anomalies, including cavernous transformation
      c. Adhesions about the portal vein, secondary to trauma, especially surgical
   2. Splenic—Banti's disease (per se)

Dunlap and others [4] have reported cases of portal hypertension due to intrahepatic block on the basis of hemochromatosis and sarcoidosis.

The common factor in the intrahepatic block is the severe fibrotic reaction associated with each type of cirrhosis. This comprises the portal vascular capacity of the liver and is the essential factor in the development of increased pressures and esophageal varices. In extrahepatic block the common factor is also a mechanical one, with the obstruction lying proximal to the liver producing the same situation, with the exception that liver disease does not complicate the picture to the same extent.

TYPES OF SURGICAL MANAGEMENT

It is understood that the aim of presently conceived operations for portal hypertension is to produce a lowered portal tension that will tend to postpone, for as long as possible, the patient's inevitable death. For a surgical procedure to be practical, the prolongation of life must surpass the tenure of the normal course of the disease without having an unreasonable increase in mortality associated with the operation. Laufman [5] has recently classified the types of surgical attack on this problem.

A. Operations Designed to Have a Delayed Effect by Promotion of Collateral Circulation.—The Talma-Morrison omentopexy has proved to be a disappointment to those who have used it. Packing gauze about the esophagus does not appear to have a rationale. In an attempt to increase the outflow tract of the liver in ascites, Madden [6] has applied magnesium trisilicate to the abraded surfaces of the liver and diaphragm to produce an artificial "bridge" between the portal and systemic circulations. No results have been reported.

B. Operations Designed to Have an Immediate Effect by Interruption of the Coronary-Esophageal Venous System.—Some British surgeons have advocated excision of the coronary vein. No results have been reported, but it is difficult to visualize a lasting effect in this instance because of numerous additional pathways to the area. Banti suggested splenectomy, but we now know that this is not a suitable procedure for two reasons: The results are not good for permanent reduction of pressure, although splenectomy temporarily decreases portal flow by about 30%, and the use of this operation precludes any attempt at a later splenorenal shunt. It is believed that a splenectomy in the presence of portal hypertension should be done only as an incidental procedure to a splenorenal shunt, unless the shunt is not technically feasible or unless for some other reason good surgical judgment contraindicates it. Ligation of the left gastric and right and left gastroepiploic arteries with their veins has been recommended but was doomed to failure. Wangensteen [7] in 1946 carried devascularization of the stomach to its ultimate by recommending near-total gastrectomy, but no results have been published. This is a very major procedure and saddles the patient with the additional burden of malnutrition. In 1947, Phemister and Humphreys [8] reported on resection of the lower esophagus and cardia of the stomach to remove the vulnerable vein-bearing area. This is a direct but radical approach to the problem and has been likened to the performance of an abdominoperineal resection for bleeding hemorrhoids, and would carry too great a mortality. Crile [9] has proposed transesophageal suture ligation of bleeding varices. This is a direct attack on the problem and a procedure of not too great magnitude. Linton [10] recently has reported on a series of 15 patients who have had this operation, and he came to the conclusion that it was a good

emergency lifesaving procedure but that its results were only temporary and that it should be followed by a more definitive procedure at a later date.

C. Attempts to Reduce Venous Inflow to the Portal System.—This includes the previously mentioned operations of splenectomy and ligation of various vessels. Massive resection of the small bowel has been tried in ascites and apparently did decrease its formation for a time, but here again it would seem that the magnitude of the procedure would make it a poor choice. To date, the most popular method for reduction of venous inflow into the liver is the portacaval shunt, which implies an anastomosis between the portal and caval systems either by a direct shunt or by using the splenic-to-renal route. These procedures, again, do not attack the basic pathological problem in the liver, but they do establish an adequate flow around the site of obstruction and from that standpoint to reduce portal pressure and lessen the likelihood of hemorrhage from esophageal varices.

D. Attempts to Reduce Intrahepatic Portal Pressure.—It is known that vasomotor factors are important in maintaining the tonus of the liver vasculature, since stimulation of the hepatic sympathetic nerve plexus will cause an appreciable rise in portal pressure. However, attempts at sympathectomy of the appropriate fibers did not reduce portal pressure. Rienhoff [11] and Berman [12] have independently explored the feasibility of arterial ligations as a means of reducing portal hypertension. The physiological rationale stems from perfusion experiments * where it has been shown that hepatic artery flow increases the resistance in the liver to portal vein flow. Berman has been able to produce reductions in portal pressure by ligation of the hepatic artery proximal to its gastroduodenal branch, the left gastric, and the splenic arteries, but it would appear that these results are only temporary. There are a number of arguments against arterial ligations:

1. The arteries of the liver after the bifurcation of the main hepatic artery are completely segmental and can be considered end arteries. Therefore, there is no possibility of a collateral arterial circulation in the liver.[16]

2. Ligation of the hepatic artery distal to its branches in the porta hepatis results almost universally in death.

3. There may be from one to five sources of arterial blood to the liver, making results of ligation of the hepatic artery completely unpredictable.[17]

4. The results of arterial ligations have been shown to lower the portal pressure only temporarily.[18]

5. The unsuccessful use of arterial ligations denies the patient the possible benefits of a shunt procedure.

6. The blood supply to regenerated liver nodules in cirrhosis has been shown to be almost exclusively arterial. With arterial ligation this regenerated tissue could be completely destroyed.[19]

E. Reduction of the Acid Factor of the Stomach.—It is fairly well recognized that gastric acid exerts a strong erosive effect on the esophageal mucosa. Chiles [20] in necropsy studies found that of 80 patients dying, of esophageal hemorrhage 45 had ulceration of the esophageal mucosa that was of primary significance in the perforation of a varix. It has, therefore, been suggested that gastrectomy, in order to remove the acid-producing portion of the stomach, might decrease the tendency of varices to bleed. This is another procedure that aims at a manifestation of the basic disease process, and its results have been disappointing.

F. Nonsurgical Means of Obliterating the Esophageal Varices.— Probably the least radical approach to the treatment of esophageal varices is the injection of sclerosing solution directly into the varix in an attempt at obliteration under direct vision through the esophagoscope. This can be done at

* References 13, 14, and 15.

multiple sittings and temporary results obtained. It is not a suitable procedure but may be indicated in very poor operative risks, in patients who refuse surgery, and in patients where operation has been unsuccessful.

INDICATIONS FOR PORTACAVAL SHUNT

Since more experience has been gained with portacaval shunting procedures, it has become obvious that numerous factors must be evaluated. The prime requisite for operation is the presence of portal hypertension, as evidenced by esophageal varices. To operate upon a patient who has not hemorrhaged requires serious consideration. It is discouraging to note that of those having their first hemorrhage, 20% will die during this first episode. Salvage of these patients depends upon prophylactic treatment or on improvement in the management of esophageal hemorrhage. Many authors believe that patients with portal hypertension will withstand surgery better than a hemorrhage, and therefore surgery is advised when the presence of varices has been determined but no bleeding has occurred. Where to draw the line remains a definite problem. Those patients with extrahepatic block will usually have a normal liver function, will usually withstand an episode of hemorrhage better, and, in turn, will tolerate surgery rather well. The patients with intrahepatic block can be classified as good or poor operative risks from the standpoint of their general status and liver function, and management must be decided upon by consideration of these factors. Frequently, their response to intensive medical therapy from the standpoint of liver function will be the deciding factor, since it cannot be expected that portacaval shunt will change the status of the liver. The presence of ascites is troublesome. Recent studies † have indicated that formation of ascites is more dependent on electrolyte and hormonal factors, associated with depressed liver function, than with the degree of hypertension or the level of the serum albumin and other such factors. The presence of ascites indicates serious liver disease, and classification of such a patient should be in the poor-risk group. Also, it has been shown that ascites can, in many instances, be controlled by rigidly limiting the salt intake. If it becomes necessary to obtain a negative salt balance, the use of the resin compounds is helpful. Habif and his group have recommended that ascites be controlled, if possible, prior to the performance of a shunt operation. In patients who have portal hypertension, have ascites, and who are bleeding, a logical method of treatment would be to attempt to control the bleeding with a Sengstaken tube, place the patient on a rigorous program to improve liver function, and institute efforts to control ascites by rigid restriction of salt intake. Operation then could be done in a more quiescent phase. If control of bleeding is not possible, the emergency stopgap procedure of transesophageal suture ligation of esophageal varices is a logical procedure, recognizing that its results are temporary but lifesaving. This also applies to those bleeding who do not have ascites. Here, again, the shunt procedure can be done during a quiescent phase. There are some who feel that arterial ligation is a suitable procedure for the treatment of ascites,[23] but we believe that to date insufficient evidence of the efficacy of arterial ligation has been recorded. Lastly, an important criterion for surgery is the recording of preoperative varix pressures. A critical level of 250 mm. of water is accepted, below which it is believed that the tendency to bleed is markedly reduced and above which surgery should be accomplished, other factors remaining the same.

CONTRAINDICATIONS TO SURGERY

Some writers believe that if a patient needs a shunt procedure it should be done, regardless of the consequences, since it represents a last grasp at further longevity. The patient should be gotten in the best possible condition prior to surgery, realizing that there is a direct relationship between increased risk in a patient and increased mortality. There

† References 21, 22.

are also other factors to be noted. Even though varix pressure and severity of disease cannot be too well correlated,[24] at least two recordings of a pressure over 250 mm. preoperatively should be shown. Otherwise, it is not considered prudent to attempt surgery, since it is believed that for bleeding due to portal hypertension to take place an elevated pressure is necessary. Also although it is less important, an elevated pressure should help in maintaining a patent anastomosis. Both Blakemore [25] and Linton [26] agree that the presence of ascites decreases the likelihood of survival. They also believe that the following findings increase mortality significantly:

1. Serum albumin level below 3 gm. per 100 cc.
2. A 3+ or 4+ cephalin-flocculation test.
3. A prothrombin time that remains more than four seconds greater than normal after adequate vitamin K therapy.
4. A serum bilirubin level about 1 mg./100 cc.
5. A sulfobromophthalein sodium retention of more than 10% after 30 minutes.

SELECTION OF CASES FOR PORTACAVAL SHUNT OPERATION

The entire mechanism of esophageal varix hemorrhage is not known. It has been demonstrated that there is no necessarily direct relationship between the severity of the varices and the severity of the portal hypertension.[27] The pressure within the varix, however, is of major diagnostic and prognostic significance, since it is a direct reflection of the pressure throughout the portal tree. Hyatt and Smith and others have found the normal portal pressure to range between 130 and 235 mm. of water. We believe that esophageal varix or portal pressure of more than 250 mm. of water is a definite indication of portal hypertension and that pressure of less than this probably indicates that the patient's condition is due to some disease other than portal hypertension. In the latter instance portacaval shunting is not indicated. Neither are we prepared at this time to advise prophylactic shunting procedures in the absence of hemorrhage in all cases of esophageal varices. However, in cases of esophageal varices with elevated portal pressure we believe that portacaval shunt is indicated. While it is recognized that factors other than high portal tension are required to produce esophageal varix hemorrhage, the fact that approximately 20% of the patients having a first hemorrhage die at that time causes us to believe that prophylactic portacaval shunting in this group is justified.

We believe that patients upon whom portacaval shunting procedures are contemplated should have a measured esophageal varix pressure of at least 250 mm. water noted, preferably on at least two occasions.

Treatment of hemorrhage from esophageal varices at Brooke Army Hospital consists of conservative measures, including the use of the Sengstaken or Patton tube and accurate whole-blood replacement. With proper management of this sort rarely is the bleeding uncontrollable. Since the measures directly aimed at control of hemorrhage, such as esophageal vein ligation, esophagogastrectomy, or excision of the esophageal veins, all fail to control the underlying portal hypertension and, since all are formidable major operations aimed at short time palliation, we believe that surgery during this period of acute hemorrhage should be postponed, if possible, until bleeding has abated and the patient is in better condition. At that time, if the pressure has been sufficiently high to warrant it, we recommend a portacaval shunting procedure. In the occasional case in which the hemorrhage cannot be controlled by the Sengstaken tube, operative intervention may be required. During this period, the most acceptable procedure is transpleural, transesophageal ligation of the varices. In this event, a portacaval shunt is planned when the patient has adequately recovered from the acute hemorrhage and operation. It must be understood that this operation is a stopgap measure aimed at control of hemorrhage and that it does not affect the portal hypertension or prevent recurrent hemorrhage.

TECHNICAL CONSIDERATIONS

Selection of the site for anastomosis between the portal and systemic venous circulations must remain a problem of judgment. Proponents of the splenorenal shunting operation point out that this procedure does not carry with it the danger of injury to the common bile duct or the hepatic artery. This operation is simpler than a direct portacaval anastomosis, the portal flow is decreased by about 30% by the concomitant splenectomy, and there is no dangerous period of complete portal-vein obstruction or the consequent threat of mesenteric thrombosis. This last factor is used in justification of the preference for both the splenorenal and the side-to-side portacaval shunt. The advantage of total vessel flow, on the other hand, is common to both the end-to-side procedures. The prime disadvantages of the splenorenal anastomosis are that the splenic vein is somewhat smaller than the portal vein and that the anastomosis is a considerable distance from the main portal trunk and the superior mesenteric vein. Despite the absence of valves within the portal veins, the distance from the portal trunk and the small size of the anastomosis, even if technically perfect, may in some cases preclude the attainment of sufficient shunt to cause satisfactory lowering of the portal pressure.

Direct end-to-side portacaval shunt obviates the disadvantages of the retrograde decompression of splenorenal anastomosis and allows a shunt of greater flow volume than either splenorenal or side-to-side portacaval anastomosis. The greater shunt flow volume is thought to aid in the maintenance of shunt patency. The principal disadvantage of the end-to-side portacaval shunt is the total deprivation of portal blood to the liver. Knowledge of the physiologic effect of total portal bypass is incomplete.

The actual choice of procedure, however, oftentimes is dictated by the site of portal obstruction. Individual anatomic arrangement, such as large hepatic caudate lobe, may preclude side-to-side portacaval shunt, and a prehepatic portal block or cavernous degeneration of the portal vein will demand that decompression be by means of the splenic vein. Previous splenectomy or splenic-vein thrombosis, on the other hand, denies the use of this vessel. In some cases it may be necessary to utilize the superior mesenteric or other smaller veins, either alone or in conjunction with supplementary anastomoses. The use of vein grafts may also be necessary, and in some clinics this is routine procedure.

The position and size of the veins to be anastomosed require that the incision for operation be generous and the exposure complete. The most satisfactory approach is through a thoracoabdominal incision. The vascularity, secondary to the portal hypertension and to liver disease, of the structures encountered at operation and the usually difficult and tedious dissection required to liberate the veins to be anastomosed make the operation a formidable one. Once the vessels have been prepared, the anastomosis is relatively simple. Fine nonabsorbable suture material is used in a continuous, everting stitch. Care must be taken that the suture is not drawn up too tightly, lest the stoma be compromised by the purse-string effect.

Before dissection is begun and after the anastomosis is completed, venous pressures should be taken. A preshunt pressure of less than 250 mm. water in the absence of other findings of portal hypertension, such as increased vascularity of the tissues or the white, thickened appearance of the hypertensive, dilated portal vein, probably should dictate abandonment of the procedure, even though preoperative studies were thought definitely indicative of portal hypertension. Decompression of the portal bed is gradual following portacaval shunting procedures, and the pressure measured immediately after the shunt is opened is not an accurate measurement of the postoperative portal pressure. One should wait 10 to 15 minutes before measuring the portal postshunt pressure, and then one may assume that there will be still further reduction of portal tension for some time after operation. A reduction in pressure

of about 100 mm. water usually is produced at the time of operation. If, however, there is marked elevation of the postshunt tension after the shunt has been opened for several minutes, the shunt must be considered technically imperfect and correction of the defect should be undertaken.

PRESENTATION OF DATA

In the two-year period, August, 1952, through July, 1954, nineteen patients have been operated upon for portal hypertension or its sequellae at Brooke Army Hospital. Sixteen of the patients were male, and their ages ranged from 10 to 67. The average age was 42. In three cases (16%) portal hypertension was caused by extrahepatic block; one of these patients also had biliary cirrhosis (Table 1). Of the 16 cases (84%) of portal hypertension on the basis of intrahepatic portal block, 15 had been diagnosed as having Laennec's cirrhosis, and in 8 of these alcoholism also was present. The remaining case of intrahepatic block was caused by schistosomiasis.

In only two cases in the series was the preoperative esophageal varix pressure found to be less than 250 mm. water, and in two other cases pressures were not taken preoperatively. In one case the patient's chief complaint was splenomegaly with splenodynia. Percutaneous splenic venography was performed at the operating table in this case and the patient treated by splenorenal shunt. In another case the patient was a 10-year-old boy with portal hypertension on the basis of omphalitis in infancy. The two remaining patients both were operated upon as emergencies, since control of hemorrhage was not being effected by more conservative measures.

Ascites was present in 3 of the cases in the intrahepatic group, and in 15 of the cases hemorrhage had occurred. In the extrahepatic group two of the patients had hemorrhaged, and in none was ascites a factor.

A portacaval shunting procedure was planned for 18 of the patients. Technical difficulties (portal vein represented by a fibrous cord) led to abandonment of the planned procedure in one case. In another, the portal pressure measured only 194 mm. water pressure, despite a preoperative esophageal varix pressure of 305 mm. water. Since the findings at this operation, including the appearance of the portal vein, did not indicate portal hypertension and since the measured venous pressure was within normal limits, only exploration was accomplished. The marked discrepancy in these pressure measurements was not explained. Both these patients died in liver coma, without hemorrhage, a short time after exploration. In two cases splenectomy alone was performed. In each case a splenorenal shunt was planned, but in one case technical difficulties, brought about by the patient's bleeding tendency and her poor general condition, dictated rapid termination of the operation, before the anastomosis could be performed. In the other case the splenic vein did not exist as such but consisted of a plexus of veins which did not lend itself to anastomosis. In only two cases was hemorrhage uncontrollable by the usual conservative measures. In one of these cases esophageal varix pressure was only 240 mm. of water, and, therefore transesophageal vein ligation was performed. Although the patient had no evidence of postoperative hemorrhage, his death from liver coma followed the operation by less than 48 hours. The remaining case will be discussed subsequently.

Fourteen cases were treated by shunting procedures. Splenorenal and side-to-side portacaval anastomoses were performed once each; the pressure changes and results in these 2 cases were not appreciably different from those in the 12 cases in which the end-to-side portacaval anastomoses were used (Table 2).

Preoperative pressures from the esophageal varices ranged from 210 to 425 mm. of water and after the shunting procedure from 120 to 185 mm. water. In five of the cases no varices could be visualized at postoperative esophagoscopy. Varix pressures measured preoperatively averaged 320 mm. water. The

TABLE 1.—*Patients Operated on for Portal Hypertension*

Case	Operation	Cause of Portal Hypertension	Date of Operation	Age, Yr.	Sex	Pre-operative Hemorrhage	Pre-operative Ascites	Remarks and Postoperative Follow-Up
1	End-to-side portacaval shunt	Cirrhosis	.....	..	M	+	—	Postoperative esophagoscopy—no varices seen; no further hemorrhage
2	End-to-side portacaval shunt	Cirrhosis	9/ 5/52	51	M	+	—	Esophagoscopy July 54—no varices seen; no further hemorrhage
3	End-to-side portacaval shunt	Cirrhosis	9/17/52	42	M	+	—	Esophagoscopy April 53—no varices seen; no further hemorrhage
4	End-to-side portacaval shunt	Cirrhosis	10/10/52	47	M	+	—	Esophagoscopy Nov. 53—no varices seen; no further hemorrhage; died Dec. 53 after operation for cerebral aneurysm; shunt open at autopsy
5	End-to-side portacaval shunt	Cirrhosis	11/17/52	25	F	+	—	No further hemorrhage; varix pressure 120 mm. on 12/8/53
6	End-to-side portacaval shunt	Cirrhosis	2/25/53	44	M	+	—	No further hemorrhage; postoperative varix pressure 180 mm.
7	End-to-side portacaval shunt	Cirrhosis	2/27/53	45	M	—	—	Developed ascites and died of liver failure 5/23/53 (3 mo. postop.); shunt closed at autopsy
8	End-to-side portacaval shunt	Cirrhosis	7/21/53	67	M	+	+	Continued hemorrhage and ascites postoperatively; died 8/13/53 (1 mo.); shunt open at autopsy
9 *	End-to-side portacaval shunt	Cirrhosis	10/16/53	55	F	+	—	Shunt unsuccessful due to thrombosis; subsequently re-operated on
10	End-to-side portacaval shunt	Cirrhosis	12/31/53	37	M	+	—	No further hemorrhage; postoperative varix pressure 160 mm.
11	End-to-side portacaval shunt	Hepatic schistosomiasis	2/24/54	23	M	—	—	No further hemorrhage; postoperative varix pressure 160 mm.
12	End-to-side portacaval shunt	Cirrhosis	6/ 3/54	47	M	+	—	No further hemorrhage; esophagoscopy 1/21/55; no varices seen
13	Side-to-side portacaval shunt	Cirrhosis	8/27/52	54	M	+	—	Died 14 mo. postoperatively of liver failure; shunt open at autopsy
14	Splenorenal shunt	Idiopathic splenic vein obstruction	10/14/53	38	M	—	—	No further hemorrhage; postoperative varix pressure 120 mm.
15	Splenectomy	Surgical injury portal vein and common duct	2/ 2/53	44	F	+	—	No further hemorrhage; postoperative varix pressure 445 mm.
16	Exploration only	Omphalitis	11/21/52	10	M	+	—	No further hemorrhage
17	Exploration only	Cirrhosis	10/ 3/52	46	M	—	+	Died in liver failure at 1 mo. postoperative
18	Exploration only	Cirrhosis	10/../52	46	M	+	+	Died in liver failure postoperatively; failure 2 mo.
19	Transesophageal varix ligation	Cirrhosis	8/ 7/53	..	M	+	..	No further hemorrhage; died liver failure 2 mo.
9 *	Esophagogastrectomy	Cirrhosis	1/../54	55	F	+	—	No further hemorrhage

* Listed twice.

TABLE 2.—*Results of Portacaval Shunting Procedures*

Case	Operation	Preoperative Varix Pressure, Mm. Water	Operative Preshunt Pressure, Mm. Water	Operative Postshunt Pressure, Mm. Water	Postoperative Varix Pressure, Mm. Water*	Difference Pre- & Postshunt Pressures	Difference Pre- & Postvarix Pressures	Apparently Good Shunt at Operation	Operation May Have Contributed to Death	Operation Apparently Aided Patient
1	End-to-side portacaval shunt	320	—	240	100	—	—220	Yes	—	Yes
2	End-to-side portacaval shunt	320	—	—	100	—	—220	Yes	—	Yes
3	End-to-side portacaval shunt	360	340	260	100	— 80	—260	Yes	—	Yes
4	End-to-side portacaval shunt	425	455	372	100	— 73	—325	Yes	No	Yes
5	End-to-side portacaval shunt	340	408	299	120	—109	—220	Yes	—	Yes
6	End-to-side portacaval shunt	345	420	380	180	— 40	—165	Yes	—	Yes
7	End-to-side portacaval shunt	345	418	280	—	—138	—	Yes	Yes	No
8	End-to-side portacaval shunt	—	400	290	—	—290	—	Yes	Yes	No
9	End-to-side portacaval shunt	280	320	400	375	+ 80	—	No	—	No
10	End-to-side portacaval shunt	300	300	—	160	....	—140	Yes	—	Yes
11	End-to-side portacaval shunt	340	494	422	160	— 72	—180	Yes	—	Yes
12	End-to-side portacaval shunt	280	250	130	100	—150	—180	Yes	—	Yes
13	Side-to-side portacaval shunt	284	325	140	160	—185	—124	Yes	No	Yes
14	Splenorenal shunt	210	305	255	120	—110	— 90	Yes	—	Yes

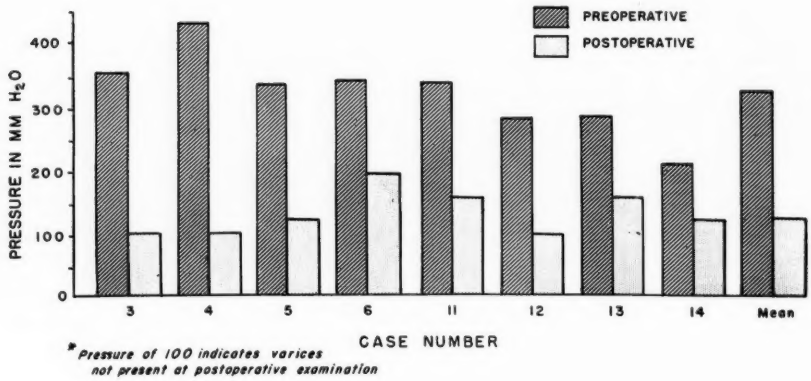
* Pressure of 100 mm. water indicates that no varices are seen on esophagoscopy.

postoperative mean varix pressure was 127 mm. water. In 10 cases pressure measurements were taken from the portal vein or from one of the larger tributaries at the beginning of the operation and after completion of the anastomosis. The mean preshunt pressure was 396 mm. of water, and the mean postshunt pressure was 283 mm. of water.

In eight cases measurements were made both from the esophageal varices and from the portal vein of its larger intra-abdominal tributaries before and after the shunt had been performed (Charts 1 and 2). In general, the decrease in pressure is more marked in the varix than in the portal vein. Nardi [28] has shown that the pressure drop as measured at operation is not an accurate indication of reduction in hepatic blood flow and that portal pressure continues to fall for some time after operation. This difference is, no doubt, due to the fact that the portal postshunt measurement is made immediately after the anastomosis has been completed, before the venospasm has relented, and before the clamped portal system has had time to empty itself. By the time postoperative esophagoscopy is performed, it is believed that the anastomosis has become more functional and that pressure within the entire portal circulation likewise has decreased. Repeated postoperative measurements have shown gradual pressure reductions. In some cases marked disparity was noted and probably was due to the fluctuations of pressure reported by Palmer. At operation the pressure in the portal system dropped an average of 113 mm. of water, the range being 40 to 200 mm. of water. The mean drop in varix pressure was 183 mm. of water, with a range of 90 to 325 mm. of water.

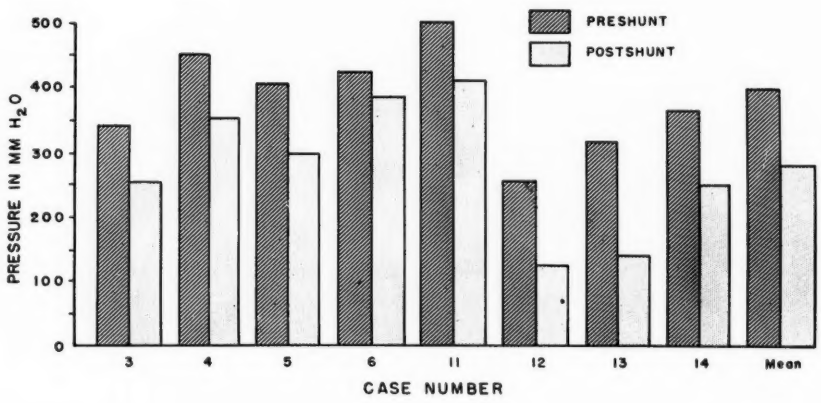
Four of the fourteen patients upon whom portacaval shunting operations were performed have died. In one case the shunt was found closed at autopsy, three months after operation, despite a portal pressure drop at operation from 418 to 280 mm. of water. One other patient died after recurrent hemorrhage from esophageal varices. Both deaths were believed to have been hastened by

CHART 1. PRE AND POSTOPERATIVE VARIX PRESSURES *



* Pressure of 100 indicates varices not present at postoperative examination

CHART 2. PRE AND POSTSHUNT PORTAL PRESSURES



operation. Two of the patients died 14 months after operation. In one case autopsy was not obtained, and in the other the death was from ruptured cerebral aneurysm. Neither patient bled from varices postoperatively. One other patient has had a recurrent hemorrhage after an unsuccessful shunt because of old portal thrombosis. Her postoperative esophageal varix pressure was 375 mm. of water, an elevation of 95 mm. above the preoperative measurement. At operation the portal vein did not flow freely, and the success of the shunt was questioned. Sodium morrhuate injections into the varices were without avail, and another operation was planned. A splenectomy had been performed in 1948, precluding the use of the splenic vein in the anastomosis. An attempt was made to perform a superior mesenteric-caval anastomosis, but at reoperation one month after the portacaval shunt this vessel also was found to be thrombosed. Omental vein pressure at this procedure was 400 mm., compared with a pressure of 320 at the first operation. Two months after this exploration the patient again had severe hemorrhage which was not well controlled by medical management. Partial esophagogas-

trectomy was performed, and on examination six months later small midesophageal varices were found. Approximately two years have now elapsed, and the patient has had no subsequent hemorrhage.

There have been two operative deaths in patients subjected to portacaval shunt, as previously mentioned, and both due to liver failure. In only one case in which shunt was accomplished was a postoperative esophageal pressure found to be more than 180 mm. of water, and in this case the shunt was thought at the time of surgery to be inadequate. In five cases no varices have been found at esophagoscopy after operation, and in no case has there been a return of elevated pressure in the remaining varices. It is believed that 12 of the 14 patients subjected to portacaval shunting procedures and one patient who underwent partial esophagogastrectomy have been benefited by their operations.

SUMMARY AND CONCLUSIONS

The etiology of portal system block, types of surgical management of portal hypertension, and the selection of cases for operation have been discussed.

The only beneficial effect of portacaval shunting operations is reduction of portal venous pressure, and this therapy for esophageal hemorrhage, even from esophageal varices, cannot be expected to be efficacious if the hemorrhage is due to causes other than portal hypertension. An esophageal varix pressure of more than 250 mm. water, on the other hand, is a definite indication of portal hypertension, and a patient with this finding should be aided by a shunting procedure. Treatment of esophageal hemorrhage by means of esophageal vein ligation, esophagogastrectomy, or other operations aimed directly at obliteration of the offending varix should be reserved for those cases in which portal hypertension does not play a part, has been controlled, or is not amenable to correction by portacaval shunting operations or in the occasional case in which hemorrhage cannot be controlled by conservative measures.

This paper includes a report of 19 patients operated upon for portal hypertension at Brooke Army Hospital between August, 1952, and July, 1954. Venous shunts between the portal and systemic circulations were constructed in 14 cases. Effective portal pressure reduction was produced in all but one case in which thrombosis of the major veins of the portal system precluded the establishment of an adequate shunt. This patient subsequently underwent partial esophagogastrectomy and has had no recurrence of hemorrhage. Operative mortality in the 14 patients who had a shunt established was 14% (2 cases). Two other patients died 14 months after shunt, one of liver failure and one of a ruptured cerebral aneurysm. In the 19 patients, counting early and late deaths from all causes and including those in whom exploration only was accomplished, the total case fatality rate is 37%, with 18- to 36-month follow-up.

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Resection of Carotid-Body Tumors with Preservation of the Carotid Vessels

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It is the purpose of this presentation to emphasize the feasibility of removing carotid-body tumors without sacrifice of the carotid arteries when the tumors are in intimate association with the carotid vessels.

LIFE HISTORY OF CAROTID-BODY TUMORS

Since there have been no reports of spontaneous regression of carotid-body tumors, one must be prepared to accept the complications produced by a slow-growing tumor in this location if removal is not advised. The gradual growth of these tumors, encircling certain vital structures and distorting and pushing others aside, may produce serious symptoms and even death in some cases. Certainly, such tumors can become very large when left untreated.*

Keen and Funke in 1906, discussing the growth characteristics of carotid-body tumors, recognized that, in general, they are benign but that some tumors, after exhibiting a slow rate of growth over a period of several years, suddenly change to a very rapidly growing neoplasm. DaCosta reported one case in which the tumor had been observed without change for 15 years but then suddenly more than doubled its size in the last six months of the observation period. Although there have been dissenting opinions in the past [17] regarding the pathologic nature of these tumors, it is generally accepted that they are usually benign tumors † with a rare case showing metastasis.‡

CONSIDERATIONS IN TREATMENT

There has been no general agreement among either clinicians or surgeons as to the proper handling of carotid-body tumors. The use of irradiation therapy, whether radium or x-ray, has been of little help in controlling the growth of these tumors, and there have been no reports of cure after its use.§ Monro expressed the consensus regarding x-ray therapy when he stated, "Radiotherapy has proved effective in a few cases, but in so small a number as to exclude its use as a treatment of choice, and to render its routine use as an adjuvant to surgery unjustifiable."

Complete removal of the tumor would seem ideal treatment except that the high operative mortality rate reported in the past is sufficient to cause concern to the surgeon. This high mortality rate has resulted from many factors. Among these are operative and postoperative hemorrhage, pneumonia, postoperative infections, and cerebral ischemia resulting from ligation of the carotid arteries when resort is made to this procedure in removing the tumor. This last is probably the most important consideration. Monro, in a review of 253 cases of carotid-

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* References 15 and 18.

† References 9, 10, 16, and 23.

‡ References 14 and 22.

§ References 17, 20, and 21.

body tumors, found that the mortality rate in those cases in which ligation of the common or the internal carotid artery or both was performed during operation was 29%, whereas in those cases in which the tumor was dissected out with preservation of the arteries the mortality rate was only 6%.

MacComb, in a series of 10 patients on whom operation was performed for carotid-body tumor, reported no deaths in three cases in which resection was performed without damage to the carotid vessels but had four postoperative deaths in seven cases in which ligation of the common or the internal carotid artery or both was performed with removal of the tumor.

Pettet and associates in a study of carotid-body tumors at the Mayo Clinic found that in 18 cases in which the tumor was resected without damage to the carotid vessels there was not a single postoperative death or complication. In nine cases in which it was necessary to ligate the common or internal carotid vessels there was a 30% mortality rate and, in addition, two cases of residual cerebral damage.

There is reason to believe that many, and perhaps all, carotid-body tumors can be removed with preservation of the carotid vessels. Gordon-Taylor has stressed this and has suggested that by careful dissection one may discern a cleavage plane, which he termed a "white line," between the tumor and the vessel. Dissection in this line of cleavage enables one to remove the tumor without damage to the vessels. A limited experience with removal of these tumors and preservation of the vessels is presented in support of this belief.

TECHNIQUE OF OPERATION

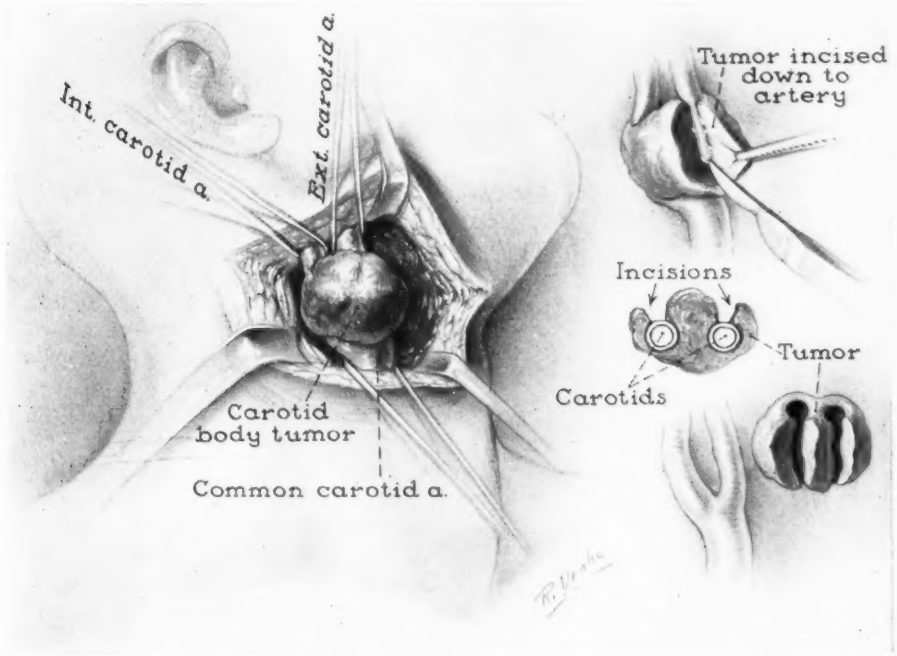
The operation requires a wide exposure of all of the tissues in the area of the procedure. This can be obtained through a long transverse incision over the tumor mass, with wide reflection of the skin flaps. Dissection is carried down in the usual fashion to the carotid-body tumor. The common carotid artery is isolated proximal to the tumor, and a tape is passed around it for temporary control, should this become necessary. The internal carotid artery is dissected out distal to the tumor, if this is feasible. On some occasions the tumor extends so high in the neck that it is difficult and, indeed, impossible to isolate the internal carotid artery until rather late in the dissection. Usually the external carotid artery distal to the tumor is easily identified and dissected out. The location of the vagus nerve, the hypoglossal nerve, and, on occasions, the glossopharyngeal nerve must be identified in order that their preservation during the later stages of the dissection may be accomplished.

It is then advisable to separate the tumor from the soft tissues as well as possible, in order that the tumor and the carotid vessels may lie relatively free in the operative area. In some cases the removal of the tumor with preservation of the carotid vessels then becomes simple. In the cases herein presented, however, the tumor actually surrounded a portion of the carotid vessels, as is so often the case. The separation of the tumor from the carotid vessels then becomes the crux of the operative problem. This can be done, however, by careful sharp dissection, a sucker being used to keep the field devoid of blood during all phases of the dissection. A cleavage plane is found between the tumor and the vessel wall along which one can proceed to separate the tumor from the carotid artery. As the dissection proceeds, it is apparent often that the tumor must be actually split on its anterior aspect so that it can be removed from the vessel that it encircles (Figure). This is accompanied by some bleeding, but with the use of a sucker and careful dissection accurate work can be done. After the tumor has been split, it is usually relatively easy to complete the dissection of the tumor away from the internal and external carotid vessels and to remove it *in toto*.

It is probably advisable always to have a preseved arterial graft available when one is operating on carotid-body tumors. Our experience to date, although limited, suggests that the use of such grafts may not be neces-

sary, for accurate removal of the tumor with preservation of the carotid vessels, even when they are encircled by the tumor, seems very feasible.

After removal of the tumor, it has been noted in our cases that the internal carotid artery is very much narrowed and obviously in spasm. For this reason we have injected ¼ grain (0.016 gm.) of papaverine hydrochloride directly into the internal carotid artery at the conclusion of the operative procedure. There have been no postoperative cerebral complications in the cases reported.



Schematic representation of technique of removal of carotid-body tumor surrounding carotid vessels. See text.

REPORT OF CASES

CASE 1.—A woman aged 39 years was seen at the Mayo Clinic because of a tumor in the right side of her neck and dizzy spells associated with sudden movements of the head. Two years previously she had had sinusitis followed by generalized lymphadenopathy. After one month all nodes regressed, except that one lump in the right submaxillary area persisted. It had not been painful but had gradually increased in size. Physical examination revealed a mass in the right side of the neck just at or above the bifurcation of the carotid vessels, about 2 in. (about 5 cm.) in diameter. The pharynx and nasopharynx were normal, and the results of examination were otherwise negative.

Operation.—Through a long transverse incision in the right submaxillary region, a tumor 4 by 4 by 3 cm. in diameter, lying in the carotid bifurcation, was identified. By careful dissection in the manner described, the tumor was removed without damage to the arteries. After the tumor had been excised, papaverine hydrochloride, ¼ grain (0.016 gm.), was injected into the vessel to control spasm. There were no postoperative complications, and the patient left the hospital on the fourth postoperative day. Examination three weeks later revealed a well-healed incision, and there was no evidence of neural or cerebral damage.

CASE 2.—A woman aged 42 years was seen at the Clinic complaining of a mass in the right side of her neck, which caused dull pain in the right side of her neck and face. She had first noted the mass 10 months previously and had been told that it was from an infected tonsil. It had not grown any since it was first noted. The results of physical examina-

tion were normal, except for a movable, rounded mass in the right upper cervical region, about 1½ in. (about 4 cm.) in diameter.

Operation.—Through a transverse incision over the tumor mass, a carotid-body tumor was identified. Clean dissection and removal of the tumor without damage to the vessels or nerves were done. There was a right hypoglossal weakness of one day's duration; otherwise, there was an uneventful convalescence. The patient was dismissed from the hospital on the fourth postoperative day. The results of examination 33 months later were normal.

CASE 3.—A man aged 40 years came to the Clinic because of a tumor in the left upper cervical region of 10 years' duration. The tumor had gradually increased in size since it had been first noticed. It produced a tight, squeezing sensation in the left side of the neck and face. On occasions, the patient had experienced some lightheadedness. A specimen of the tumor taken elsewhere three years previously for biopsy had been diagnosed "sclerosing hemangioma." The tumor continued to grow, and about six months prior to the time when the patient came to the Clinic a cellophane band had been placed around the left common carotid artery preparatory to resection of the tumor. This operation had been followed by a paralysis of the left side of the patient's face and complete loss of voice, which had cleared up to a present state of severe hoarseness. Examination showed a mass about the size of a lemon in the left side of the neck at the bifurcation of the carotid vessel. The mass pulsated, and pressure over it caused faintness. Further examination revealed fixation of the left vocal cord. Microscopic sections of the biopsy specimen taken three years previously were obtained and were interpreted to indicate carotid-body tumor.

Operation.—A long vertical incision was made excising the old scar, and a large carotid-body tumor was identified. The common carotid artery was identified, and the tumor was dissected away from it up to the bifurcation. The external carotid artery was divided at the upper margin of the tumor. The tumor was then dissected away from the internal carotid artery, the tumor being split as the dissection proceeded upward. Several small rents made in the vessel during the dissection were repaired with fine silk. The hypoglossal nerve went through the tumor and was sacrificed. The vagus nerve had been taken at the previous operation. Although the tumor extended up to the base of the skull, it was all excised. Two pieces of cellophane tape were removed from around the common carotid vessel. There was no evidence that the band had appreciably decreased the size of the lumen of the vessel. Papaverine hydrochloride, ¼ grain (0.016 gm.), was injected into the common carotid artery at the end of the surgical procedure. The postoperative course was uneventful, except for some difficulty in swallowing as a result of paralysis of the muscles of the left side of the tongue. There were no signs suggestive of cerebral ischemia postoperatively.

COMMENT

There is defense for the practice of leaving in situ carotid-body tumors intimately associated with the carotid-artery bifurcation and internal carotid artery, although treatment in the cases herein reported was not predicated on this concept. There can be little defense for resection of the tumor and ligation of the common, external, and internal carotid arteries. This is true in spite of numerous ingenious procedures recommended as making ligation safe. Dandy has recommended partial closure of the common carotid artery with strips of fascia lata prior to ligation. Some have recommended intermittent arterial obstruction before proceeding with ligation. The application of aluminum and cellophane bands and the use of special clamps have been championed by various surgeons. Pemberton and Livermore and MacComb have used—and recommend—administration of anticoagulants following ligation of the carotid vessels. This, of course, is fraught with certain dangers well known to those who have used anticoagulants after extensive surgical procedures.

Excision of a portion of the internal carotid artery or of the carotid bifurcation has led to the development of several methods of reconstruction. Enderlen reported a case in which the bifurcation of the carotid artery was resected with the tumor. The external carotid was ligated and the common carotid was anastomosed to the internal carotid. The patient recovered without evidence of cerebral damage. Gage || and Shea and Harrison have reported individual cases in which the common carotid has been anastomosed to the internal carotid artery with successful results following resection of the carotid bifurcation.

That homografts may be used to bridge defects in small arteries has been demonstrated

|| Gage, M., in discussion of Pemberton and Livermore.[5]

experimentally by Miller and co-workers. Recent experience in the treatment of arterial defects resulting from battle injuries has demonstrated that arterial homografts may be used successfully in restoring arterial circulation when used to replace irreparably damaged arteries of the extremities.[7] Conley has used vein grafts to replace resected portions of the internal and common carotid arteries.

In spite of the value of these reconstructive measures, preservation of the vessels as described in the cases reported would seem preferable in the removal of carotid-body tumors.

SUMMARY

Three cases illustrating removal of carotid-body tumor and preservation of the carotid vessels, in spite of intimate attachment of tumor to vessels, are presented. The operative technique is discussed and illustrated. The relation of this to other methods for treating carotid-body tumor is discussed.

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Observations on Liver Blood Flow

Its Relationship to Cardiac Output in Anesthetized and Unanesthetized Animals

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Ten years have elapsed since Bradley [1] first reported measurement of estimated hepatic blood flow (EHBF) using the sulfobromophthalein sodium (Bromsulphalein, BSP) method. In the intervening decade the basic principles upon which the technique is dependent have been the subject of numerous appraisals. Many have been critical of the accuracy obtained,* whereas others have substantiated the reliability of the method.† In spite of the controversy, its use in the study of the hemodynamics of the liver under various experimental conditions and in disease has gained impetus. The measurement of EHBF in cirrhotics ‡ following experimental hemorrhage,§ after arterialization of the liver,[15] during anesthesia [16] and drug administration,|| and subsequent to portacaval shunt ¶ are but a few of the situations where it has been utilized.

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* References 2-7.

† References 8-11.

‡ References 12 and 13.

§ References 8, 14.

|| References 17 and 18.

¶ References 19 and 20.

Prior to introduction of the sulfobromophthalein sodium method, techniques for measurement of hepatic blood flow were cumbersome and impractical for use in the human, for they required extensive surgical manipulation. Most popular was the use of the thermostromuhr technique, as described by Burton-Opitz in 1911 # and subsequently reported upon by the others listed in Table 1. A review of the eight publications reporting measurement of liver blood flow by this method reveals such variability in techniques and conditions under which observations were made as to make comparison of findings difficult. The preliminary ligation of the inferior vena cava below the diaphragm, the assumption that the value for blood flow is the summation of portal vein and hepatic artery flows in separate series of animals, the variability in positioning of the thermostromuhr, and such comments as, "We do not claim that the figures for the volume flows recorded here are absolute—the thermostromuhr is not a precision instrument," [23] tend to reduce the meaning of the results obtained. In approximately 100 observations on 42 animals, compiled from the literature, the mean blood flow by this method was 24 ml/kg/min. In all series individual variations were great. No difference was found between animals anesthetized or unanesthetized.

Another means of measurement of hepatic blood flow was by the direct collection of blood coming from the hepatic veins per unit of time, as reported by MacLeod and Pearce [24] in 1914 and Blalock and Mason [25] in 1936. The former authors found a mean blood flow of 44 ml/kg/min. in 7 animals anesthetized with ether, whereas the latter

References 21 and 22.

authors obtained a value of 28.6 ml/kg/min. for 10 unanesthetized dogs. Recently (1954), Selkurt,[10] using a method for direct collection which permitted simultaneous comparison with the sulfobromophthalein sodium method, reported the liver blood flow to be 33 ml/kg/min. when pentobarbital was used as the anesthetic agent. This value was 7.3% lower than the flow obtained by the indirect method. All variations of the direct collection technique of necessity interfere with normal circulatory hemodynamics so as to make questionable the physiological nature of the results obtained.

The method of measurement of hepatic blood flow utilizing urea output, described by Lipscomb and Crandall in 1947,[26] has been found to be less suitable for clinical use than the sulfobromophthalein sodium method because of the uncertainties of analysis.[11] By this method a mean blood flow of 32 ml/kg/min. was obtained in the dog.

The plasma clearance of rose bengal by Simpson and Saperstein,[27] who obtained a mean EHBF of 31.5±4.1 ml/kg/min. for 18 dogs, and the rate of disappearance of colloidal chromic phosphate from the blood of normal young men, as described by Dobson,[28] are methods that merit further consideration.

Since introduction of the sulfobromophthalein sodium method of studying blood flow, there have been 13 publications in which normal values for EHBF in the dog have been presented (Table 1). In 10 publications values were for animals under pentobarbital anesthesia; in one, chloralose, and in two, unanesthetized. In reviewing the results, it was discouraging to find that under fairly comparable experimental conditions there was great variation in the average values representing normal hepatic blood flow. The values ranged from the mean of 30 ml/kg/min. in four separate series by Smythe and co-workers to 56 ml/kg/min. in Hallett and Schilling's group of 14 animals. Likewise, reports of the anesthetic effect upon hepatic blood flow are variable. Habif [29] and Shackman [30] reported a decrease in hepatic flow in man following thiopental and cyclopropane anesthesia, whereas Pratt [16] found normal or greater values following cyclopropane and pentobarbital (Nembutal) in the dog. Pratt also reported that either anesthetic produced either no change or a decrease in blood flow, although no data are presented.

In this laboratory during the last two years the sulfobromophthalein sodium technique has been utilized for the measurement of hepatic blood flow in the dog under various conditions. It was important that the "normal" blood flow be evaluated so that the effect of certain experimental procedures might be determined. Because of the differences reported in the literature for normal EHBF, we feel justified in reporting our experiences. Values are presented for blood flow and splanchnic oxygen consumption in 16 unanesthetized dogs, in 20 dogs anesthetized with pentobarbital, and in 10 dogs during ether anesthesia.

It has been estimated that approximately one-fourth of the cardiac output passes through the liver each minute. Until recently this situation was based upon nonsimultaneous determination of hepatic flow and cardiac output.* Concomitant measurement of cardiac output and EHBF was made on anesthetized animals by Werner, MacCanon, and Horvath [34] and by Smythe, Heinemann, and Bradley,[11] the former finding the EHBF to be 32±11% of the cardiac output; the latter reporting it to be 31% in six animals. Perusal of their data, however, shows eight animals having liver blood flows varying from 7% to 43% of the cardiac output.

Simultaneous determinations of cardiac output were made by us in all dogs anesthetized with pentobarbital and in eight of those unanesthetized. The results are included in this report.

METHOD

Forty-six male and female mongrel dogs averaging 11.1 kg. were used. All were fasted for 12 hours but were permitted water ad libitum. Twenty were initially anesthetized with 25 mg. of pento-

* References 31-33.

TABLE 1.—*Measurements of Hepatic Blood Flow in the "Normal" Dog*

Author	Date	Number of Animals	Number of Observations	Technique	Anesthesia	Liver Blood Flow	
						Mean Ml/Kg/Min.	Range Ml/Kg/Min.
Burton-Opitz [21,22]	1911	15	?	Stromuhr	Ether	25	.....
McLeod & Pearce [24]	1914	7	7	Collection	Ether	44	26-85
Grab, Janssen & Rein [48]	1929	5	5	Stromuhr	None	25	22-43
Grab, Janssen & Rein [49]	1929	6	6	Stromuhr	None	25	18-33
Herrick, Mann, Essex & Baldes [51]	1934	1	3	Stromuhr	None	62*	52-71
		..	3	Stromuhr	None	103†	84-114
Blalock & Mason [25]	1936	10	13	Collection	None	28.6	18.7-39
Soskin, Essex, Herrick & Mann [52]	1938	1	3	Stromuhr	Amytal	24.1	23-25
Grindlay, Herrick & Mann [50]	1941	8	66	Stromuhr	Pentobarbital	24	16.8-30
		2	2	Stromuhr	None	22	.....
Grodins, Osborne, Ivy & Goldman [28]	1941	5	14	Stromuhr	Pentobarbital	15.5‡	5-37
		21	46	Stromuhr	Pentobarbital	6.6§	2.3-13.8
Lipscomb & Crandall [26]	1947	20	20	Urea output	None	32	18-48
Werner & Horvath [7]	1952	17	49	Sulfobromophthalein	Pentobarbital	42±2.9	16-111
Werner, MacCanon & Horvath [34]	1952	14	41	Sulfobromophthalein	Pentobarbital	40	.....
Hallett & Schilling [20]	1952	14	14	Sulfobromophthalein	Pentobarbital	56	31-93
Pratt, Burdick & Holmes [9]	1952	14	51	Sulfobromophthalein	None	48.6±9.9	37.7-65.4
Heinemann, Smythe & Marks [8]	1953	9	9	Sulfobromophthalein	Pentobarbital	27.6±5	16-36
Smythe, Heinemann & Bradley [11]	1953	26	26	Sulfobromophthalein	Pentobarbital	29.5±9.3	11.6-49.4
Smythe, Gilmore & Handford [17]	1953	27	27	Sulfobromophthalein	Pentobarbital	32±11.5	14-57
Selkurt [5]	1953	9	63	Sulfobromophthalein	Pentobarbital	35.4	21-55
Bollman, Khattab, Thors & Grindlay [30]	1953	?	35	Sulfobromophthalein	None	42.5±0.9	.....
Casselman & Rappaport [45]	1954	21	33	Sulfobromophthalein	Pentobarbital	37±2.3	.....
Selkurt [10]	1954	14	274	Sulfobromophthalein	Pentobarbital	35	.....
		..	..	Direct	Pentobarbital	33	.....
Hamrick & Myers [14]	1955	13	13	Sulfobromophthalein	Chloralose	47±4.8	27-79
		5	5	Sulfobromophthalein	Chloralose	52±16.6	20-86
Smythe & Gilmore [18]	1955	14	14	Sulfobromophthalein	Pentobarbital	30±11.5	16-50
Simpson & Saperstein [27]	1955	10	10	Rose bengal	Pentobarbital	31.5±4.1	.....
Fisher, Russ, Selker & Fedor	1955	20	20	Sulfobromophthalein	Pentobarbital	49±7.4	36-65
		10	10	Sulfobromophthalein	Ether	70±4.1	52-86
		20	20	Sulfobromophthalein	None	45±9.3	34-70

* Fasted.
† Fed.
‡ Portal.
§ Hepatic artery.

barbital sodium per kilogram of body weight and were maintained at a surgical level of anesthesia by supplements of more anesthetic agent as needed. All blood flows were determined between one and one-half and two and one-half hours after the onset of anesthesia. Ether was administered to 10 dogs by the open-drop method, and effort was made to maintain a plane of anesthesia comparable with that of the animals receiving pentobarbital. Determinations were made in 16 animals without anesthesia. In this group the skin was infiltrated with procaine to permit insertion of cannulae.

Blood flows were determined by a technique similar to that of Bradley and others. Under fluoroscopic guidance a No. 9 ureteral catheter was inserted via the right external jugular vein as deeply into a left hepatic vein as would permit withdrawal of blood. At the same time a similar catheter was passed into the right ventricle so that its tip was at the orifice of the pulmonary artery. During the course of the experiment, patency of these catheters was maintained by dripping heparinized † saline solution through them at a rate of four to six drops a minute. Several inches of polyethylene tubing was threaded into a leg vein, and a polyethylene catheter was inserted into the femoral artery. In order to raise the plasma level rapidly and to shorten the time for equilibration, a priming dose of 2 mg. of sulfobromophthalein sodium per kilogram of weight was administered to all dogs. Immediately after this, sulfobromophthalein sodium solution at a rate of 1 to 2 mg/min. was injected by means of a constant perfusion pump [35] through the small polyethylene catheter. Using heparinized syringes, we began sampling after 30 minutes of perfusion, peripheral and hepatic vein blood samples being taken at accurately timed 10-minute intervals until three or four pairs were drawn. An aliquot of injected sulfobromophthalein sodium solution was taken for determination of the actual rate of administration. Sulfobromophthalein sodium concentration in plasma was determined using the Coleman Junior Spectrophotometer at a wave length of 565 mμ, and the hematocrit value was determined from each peripheral blood sample by the Wintrobe technique. Estimated hepatic blood flow was calculated in the usual manner, after Bradley, using the equation

$$EHBF = \frac{R \text{ (Rate of infusion in mg/min.)}}{0.01\ (P\text{-}H)\ \text{(1-hematocrit)}}$$

P representing the peripheral concentration of sulfobromophthalein sodium and H the sulfobromophthalein sodium concentration in hepatic vein blood. Samples for determination of oxygen content of peripheral arterial, hepatic vein, and mixed venous (cardiac) blood were collected in sealed heparinized syringes containing sufficient mercury for mixing. These bloods were drawn in all instances at the same time as the second pair of samples for measurement of EHBF (40 minutes) was withdrawn. They were stored in an ice-water bath as soon as taken and were analyzed within several hours by the manometric method of Van Slyke.[36]

Oxygen consumption was recorded by a Benedict-Roth spirometer which was connected to all anesthetized animals by an endotracheal tube with inflatable cuff. A specially devised face mask was used in the unanesthetized group. For these animals a preliminary period of conditioning to its tolerance was essential. Cardiac outputs were calculated utilizing the Fick principle. Square meter surface of animals for calculation of cardiac index was obtained from the nomogram of Cowgill and Drabkin.[37]

All data were subjected to statistical analysis utilizing Fisher's t-test.[38]

RESULTS

The results presented are for all animals upon which blood flow values were obtained and do not represent a selection. All determinations, with but a few exceptions, met the stringent requirements repeatedly proposed as being necessary to fulfill the assumptions upon which the sulfobromophthalein sodium method rests. In only one of the 46 flows was the peripheral sulfobromophthalein sodium level less than 0.5 mg. per 100 cc. the level below which determinations were discarded by Smythe.[18] Dog 159A, in the series of animals receiving ether anesthesia, exhibited a plasma level of 0.46 mg. per 100 cc. In three dogs—two with ether anesthesia, No. 95A and No. 135A, and one under pentobarbital, No. 866—peripheral plasma level of sulfobromophthalein sodium was changing (ΔP) more than the 0.00016 mg/min. tolerated by Smythe,[18] but less than the 0.0005 mg/min. allowed by Bradley.[1] The ΔP for these three animals was 0.00026, 0.00030, and 0.00030 mg/min., respectively. Correction for changing levels was made using the Bradley method, plasma volumes being estimated rather than quantitatively determined. Sulfobromophthalein sodium extraction was more than 15% in all animals, except No. 717 (unanesthetized). In this dog the EBSP was 10%, but, as the peripheral plasma level

† Heparin supplied through the courtesy of Dr. G. H. Berryman of Abbott Laboratories.

TABLE 2.—*Estimated Hepatic Blood Flow, Splanchnic Oxygen Consumption,*

Exp. No.	Dog No.	Weight, Kg.	Surface Area, Sq. M.	Hematocrit	Length Anesthesia, Min.	PBSP,* Mg/100Cc.	EBSP,† %	RBSP,‡ Mg/Min.	ΔP,§ Mg/Min.	EHBF‖ Ml/Min.	EHBF‖ Ml/Kg/Min.
1	813	10.1	0.49	43	...	0.87	46	1.50	0.00000	655	65
2	818	11.6	0.50	35	...	0.64	62	1.43	0.00000	550	47
3	816	9.6	0.49	48	...	1.67	37	1.58	0.00007	490	51
4	841	16.0	0.73	49	...	0.85	32	1.22	0.00003	866	54
5	839	13.1	0.58	38	...	0.72	55	1.25	0.00006	683	52
6	800	15.0	0.60	44	110	0.87	36	1.27	0.00000	708	47
7	832	12.3	0.50	49	125	1.50	37	1.33	0.00003	637	52
8	877	9.0	0.42	35	170	1.44	27	1.36	0.00005	541	60
9	860	11.9	0.63	40	115	1.38	27	1.31	0.00007	597	50
10	866	8.6	0.46	34	120	2.06	20	1.28	0.00030	462	54
11	868	13.8	0.61	39	95	0.85	33	1.20	0.00002	705	51
12	883	10.3	0.44	46	155	1.36	35	1.09	0.00004	425	41
13	888	16.8	0.68	42	90	0.73	41	1.15	0.00001	708	42
14	865	10.2	0.54	32	140	1.55	23	1.34	0.00001	547	54
15	783	12.2	0.52	36	130	1.18	36	1.12	0.00009	468	39
16	837	9.6	0.46	52	110	2.18	47	1.34	0.00010	339	36
17	872	12.0	0.54	34	110	1.56	28	1.46	0.00001	522	43
18	901	15.5	0.63	47	100	1.32	45	1.75	0.00005	560	36
19	814	9.6	0.51	40	95	1.66	25	1.27	0.00010	516	54
20	730	8.4	0.43	46	105	1.71	27	1.16	0.00002	447	53
N	...	20	20	20	15	20	20	20	20	20	20
Mean	...	11.8	0.54	42	118	1.32	36	1.32	0.00005	571	49
S. D.	...	....	....	±5	...	±0.50	±11.2	±0.17	±0.00002	±122	±7.4

* Peripheral plasma concentrations of sulfobromophthalein.

† % extraction of sulfobromophthalein $= \frac{\text{Arterial conc. sulfobromophthalein—hepatic vein conc. sulfobromophthalein (mg/100 cc.)} \times 100}{\text{Arterial sulfobromophthalein conc. (mg/100 cc.)}}$

‡ Sulfobromophthalein removal rate.

§ Change in peripheral concentration of sulfobromophthalein mg/ml/min.

‖ Estimated hepatic blood flow.

¶ Splanchnic.

Cardiac output.

TABLE 3.—*Estimated Hepatic Blood Flow, Splanchnic Oxygen Consumption,*

Exp. No.	Dog No.	Weight, Kg.	Surface Area, Sq. M.	Hematocrit	PBSP,* Mg/100 Cc.	EBSP,† %	RBSP,‡ Mg/Min.	ΔP,§ Mg/Min.	EHBF‖ Ml/Min.	EHBF‖ Ml/Kg/Min.
1	738	8.8	0.49	39	1.40	29	1.05	0.00006	425	48
2	732	9.3	0.50	40	0.87	39	1.30	0.00005	628	68
3	719	9.0	0.46	46	1.67	31	1.00	0.00004	357	40
4	717	11.0	0.53	42	3.65	10	1.03	0.00010	481	44
5	710	8.5	0.45	43	0.97	51	1.02	0.00002	365	43
6	703	11.1	0.54	44	0.84	46	1.00	0.00005	464	42
7	771	8.5	0.45	43	1.34	28	1.25	0.00001	585	69
8	749	12.5	0.57	44	0.98	35	1.16	0.00004	604	48
9	785	9.8	....	44	1.31	42	1.02	0.00007	331	34
10	727	10.9	....	47	1.35	40	1.06	0.00000	370	34
11	659	11.0	....	24	1.70	24	1.40	0.00000	460	42
12	655	9.0	....	34	1.60	35	1.40	0.00000	379	42
13	656	9.2	....	27	1.18	32	1.40	0.00004	505	55
14	657	9.7	....	35	1.24	37	1.27	0.00020	425	44
15	675	12.0	....	23	1.17	21	1.21	0.00002	629	52
16	707	9.8	....	55	1.86	34	1.16	0.00007	409	42
N	...	16	8	16	16	16	16	16	16	16
Mean	...	10	0.49	39	1.44	33	1.17	0.00004	463	46
S. D.	...	....	....	±8.7	±0.64	±9.8	±0.18	±0.00001	±96	±10.1

For explanation of symbols see footnotes to Table 2.

and Cardiac Output in Normal Pentobarbital Anesthetized Dogs

Oxygen, Vol. %			O_2, Vol. % Difference		Sp.¶ O_2 Consumption		Oxygen Consumption		Sp. O_2 Consumption per Total O_2 Consumption	Cardiac Output, Ml/Min.	Cardiac Index, C. O./ Sq. M.	EHBF/ C. O.,‡ %
Periph.	Cardiac	Hepatic	Periph. Cardiac	Periph. Hepatic	Ml/Min.	Ml/Kg/ Min.	Ml/Min.	Ml/Kg/ Min.				
19.5	14.9	14.0	4.6	5.5	36.0	3.5	81.4	8.0	44.2	1769	3.61	37.0
16.1	11.6	10.3	4.5	5.8	31.9	2.7	88.7	7.6	35.9	1971	3.94	27.9
22.6	19.1	16.9	3.5	5.7	27.9	2.9	65.1	6.8	42.8	1860	3.79	20.3
21.3	18.3	17.4	3.0	3.9	33.7	2.1	92.3	5.8	36.5	3076	4.21	28.1
18.3	15.2	13.7	3.1	4.6	31.4	2.0	81.4	6.2	38.5	2625	4.52	26.0
19.3	15.0	14.9	4.3	4.4	31.1	2.0	85.4	5.6	36.4	1986	3.27	35.6
22.5	17.7	18.2	4.8	4.3	27.4	2.2	71.6	5.8	38.2	1491	2.98	42.7
14.0	11.3	8.6	2.7	5.4	29.2	3.2	55.7	6.2	52.4	2063	4.91	26.2
17.4	11.2	12.2	6.2	5.2	31.0	2.6	97.6	8.2	31.8	1574	2.50	37.9
16.3	12.2	12.2	4.1	4.1	18.9	2.2	62.6	7.3	30.2	1527	3.32	30.3
17.1	11.5	9.2	5.6	7.9	55.6	4.0	109.0	7.8	51.0	1946	3.19	36.2
19.4	14.6	14.2	4.8	5.2	22.1	2.1	57.0	5.5	38.7	1187	2.69	35.8
17.7	13.6	13.7	4.1	4.0	28.3	1.7	97.6	5.8	29.0	2380	3.50	29.7
15.2	10.2	7.5	5.0	7.7	42.1	4.1	97.6	9.5	43.1	1952	3.61	28.0
15.5	12.6	10.7	2.9	4.8	22.4	1.8	67.1	5.5	33.3	2314	4.45	20.2
23.5	20.2	16.8	3.3	6.7	22.7	2.3	56.9	5.9	39.8	1724	3.74	19.7
15.1	11.7	10.6	3.4	4.5	23.4	2.0	105.8	8.8	22.1	3111	5.76	16.8
19.1	13.7	13.6	5.4	5.5	30.8	2.0	87.5	5.6	35.2	1620	2.57	34.5
18.0	14.6	14.9	3.4	3.1	16.0	1.7	65.1	6.8	24.6	1915	3.75	26.9
17.7	12.7	13.6	5.0	4.1	18.3	2.2	74.5	8.8	24.5	1490	3.46	30.0
20	20	26	20	20	20	20	20	20	20	20	20	20
18.3	14.1	13.2	4.2	5.1	29.0	2.5	80.0	7.0	36.4	1979	3.70	30.0
±2.6	±2.8	±2.8	±0.31	±1.2	±8.8	±0.72	±16.5	±1.1	±11.2	±483	±0.80	±6.8

and Cardiac Output in Normal Unanesthetized Dogs

Oxygen, Vol. %			O_2, Vol. % Difference		Sp.¶ O_2 Consumption		Oxygen Consumption		Sp. O_2 Consumption per Total O_2 Consumption	Cardiac Output, Ml/Min.	Cardiac Index, C. O./ Sq. M.	EHBF/ C. O.,‡ %
Periph.	Cardiac	Hepatic	Periph. Cardiac	Periph. Hepatic	Ml/Min.	Ml/Kg/ Min.	Ml/Min.	Ml/Kg/ Min.				
13.5	15.6	13.4	3.9	6.1	25.9	2.9	167	18.9	15.5	4282	8.73	9.9
17.6	11.4	12.0	6.2	5.6	35.1	3.7	114	12.3	30.7	1839	3.68	34.1
14.0	9.6	9.9	4.4	4.1	14.6	1.6	81	9.0	18.0	1840	4.00	19.4
20.1	13.9	13.2	6.2	6.9	30.6	2.7	122	11.0	25.0	1968	3.71	22.5
18.7	16.0	13.5	2.7	5.2	18.9	2.2	101	11.8	18.7	3741	8.30	9.8
17.7	13.6	13.7	4.1	4.6	21.3	1.9	146	13.1	14.5	3561	6.59	13.0
19.0	15.7	14.0	3.3	5.0	29.6	3.4	86	10.1	34.4	2606	5.79	22.7
19.6	13.4	13.9	6.2	5.7	34.7	2.7	106	8.5	32.7	1710	3.00	35.6
19.1	....	12.6	...	6.5	21.5	2.2	...	....	....	....	....	....
17.8	....	10.6	...	7.2	27.1	2.5	...	....	....	....	....	....
....	....	....	...	...	....	...	...	....	....	....	....	....
....	....	....	...	...	....	...	...	....	....	....	....	....
....	....	....	...	...	....	...	...	....	....	....	....	....
....	....	....	...	...	....	...	...	....	....	....	....	....
....	....	....	...	...	....	...	...	....	....	....	....	....
....	....	....	...	...	....	...	...	....	....	....	....	....
10	8	10	8	10	10	10	8	8	8	8	8	8
18.3	13.6	12.6	4.7	5.7	25.9	2.6	115	11.8	23.6	2693	5.4	20.8
±2.1	±2.3	±1.4	±1.4	±0.94	±6.8	±0.64	±29	±3.2	±8.1	±969	±2.1	±10.0

of sulfobromophthalein sodium was more than 1.0 mg. per 100 cc., this degree of extraction meets Bradley's criterion. Had these five animals been discarded, no drastic change in results would have occurred.

Results for the 20 normal animals anesthetized with pentobarbital and the 16 unanesthetized animals are presented in Tables 2 and 3. After an average of 118 minutes of pentobarbital anesthesia, the EHBF was found to be 571±122 ml/min. or, more meaningfully expressed in relation to body weight, 49±7.4 ml/kg/min. Comparing these findings with those of the unanesthetized group, we found there was no significant difference, values for the latter being 463± 95.9 ml/min., or 46±10.1 ml/kg/min. Likewise, extraction of sulfobromophthalein sodium was similar in the two groups, being 36±11.2% for the anesthetized and 33± 9.8% for the unanesthetized animals.

The 10 animals receiving ether anesthesia for an average of 93 minutes were found to have a mean hepatic blood flow of 803± 277.7 ml/min., or 70±4.1 ml/kg/min. (Table 4). The values were from 52 to 86 ml/kg/min. Although the mean extraction of sulfobromophthalein sodium, 29±9.3%, was slightly lower than in the other two groups, statistically there was found to be no difference.

No significant statistical difference was found in the oxygen contents of peripheral arterial, hepatic venous, and mixed venous blood of the two groups. Splanchnic oxygen consumption in each group was 29±8.8 ml/min. and 26±6.8 ml/min., respectively. However, since there was a difference in total oxygen consumption for these two groups (7.0±1.1 ml/kg/min. for animals under anesthesia versus 11.8±3.2 ml/kg/min. for those awake), the per cent of the total oxygen consumption utilized by the splanchnic bed differed, being 36.4±11.2% in the former and 23.6±8.1% in the latter. This increase in total oxygen consumption in the unanesthetized group may be explained by the fact that these animals were not in a complete resting state. Because of this elevated oxygen consumption, the cardiac index for the unanesthetized dogs was greater (5.4±2.1 liters) than was that for the anesthetized animals (3.7±0.8 liters). These differences in cardiac index are reflected in the estimate of the per cent of cardiac output passing through the liver per minute. This was found to be 30±6.8% for the animals receiving pentobarbital and 20.8±10.0% for those unanesthetized. In analyzing these data, it was interesting to note that four of the latter animals, Nos. 738, 710, 703, and 771, had cardiac indices which averaged 7.35 liters. Only 13.8% of the cardiac output passed through the liver of these animals, whereas in the other four, having an average cardiac index of 3.59 liters, the mean per cent was 27.9.

COMMENT

The finding of no difference in the hepatic blood flow of unanesthetized and anesthetized (pentobarbital) animals was of interest. The value obtained for the former group is similar to that obtained by Pratt [9] and by Bollman [39] in the only other reports of hepatic blood flow determined on unanesthetized animals using sulfobromophthalein sodium. It also agrees with the report of Hamrick and Myers,[14] who used chloralose "in an attempt to more nearly approach the unanesthetized state as far as circulation is concerned." The results obtained in animals under pentobarbital anesthesia for approximately two hours agree with those of Werner and Horvath ‡ and Hallett and Schilling and co-workers [20] but are greater than in all of the reports of Smythe and associates.§ The difference cannot be explained as being due to inclusion of data when the peripheral sulfobromophthalein sodium level is very low, or changing rapidly, or when the per cent of extraction of sulfobromophthalein sodium is small, as has been used by Smythe [18] to explain the higher values obtained by Werner.[7] It is probable that length and depth of anesthesia is the variable which has resulted in the dif-

‡ References 7, 34.

§ References 8, 11, 17, and 18.

TABLE 4.—*Effect of Ether Anesthesia on Estimated Hepatic Blood Flow*

Exp. No.	Dog No.	Weight, Kg.	Hematocrit	FBSP* Mg/100 Cc.	EBSP,† %	BBSP,‡ Mg/Min.	ΔP,§ Mg/Min.	Length Anesthesia, Min.	EHBF‖ Ml/Min.	EHBF‖ Ml/Kg/Min.
1.....	143A	8.3	36	1.10	22	1.02	0.00001	101	664	80
2.....	135A	9.6	49	1.20	28	1.12	0.00026	85	661	68
3.....	95A	9.6	51	3.82	15	1.44	0.00030	101	498	52
4.....	118A	12.8	52	0.81	40	1.10	0.00008	91	696	54
5.....	148A	8.4	38	1.13	27	0.86	0.00002	100	462	55
6.....	142A	7.4	48	0.82	43	1.12	0.00008	77	615	83
7.....	159A	12.0	43	0.46	41	1.11	0.00001	82	1036	86
8.....	169A	16.0	49	0.63	31	1.00	0.00001	95	1241	78
9.....	186A	16.2	49	1.18	19	1.23	0.00005	95	1053	76
10.....	193A	16.8	46	0.86	27	1.37	0.00001	90	1103	66
Mean.....		11.7	46.6	1.20	29	1.14	0.00008	92	803	70
S. D.....		....	±5.4	±0.70	±9.3	±0.17	±0.0001	..	±277.7	±4.1

For explanation of symbols see Table 2.

ference in values. None of the other reports contain data as to the length of anesthesia before blood-flow estimations. It has been demonstrated || that cardiac output becomes relatively stable only after about 90 minutes of anesthesia, and even after that time it is constantly shifting.[42] In fact, it has been recommended by Green and others,[43] on the basis of their observations, that a control period of three or four hours be allowed during anesthesia.

Thus, it is reasonable to assume that a changing cardiac output as affected by anesthesia might be reflected in a similar state of hepatic blood flow. This may be borne out by the fact that the mean cardiac index in our series, 3.7±0.8 liters, closely agrees with the 3.5 liters reported by Werner and Horvath [34] and differs, though not significantly, from Smythe's [11] value of 2.9±1.7 liters, calculated from his data using Meek's formula for estimation of surface area of the dog. Likewise, the simultaneously performed estimations of liver flow done by us and by Werner are in agreement but are approximately one-third greater than those of Smythe. In spite of this difference, the hepatic blood flow simultaneously determined has been found by these authors and by us to be 30% of the cardiac output. This is possible in Smythe's series, in spite of the difference in the value of the hepatic blood flow, because of the extreme range for both cardiac output and blood flow in the six dogs. His values for cardiac outputs were from 1.2 to 4.4 L/min., whereas the hepatic flow ranged from 20 to 49 ml/kg/min., and, although the mean EHBF per cent of cardiac output was 30.8 for his six animals, the actual values were quite variable, being 28%, 33%, 43%, 8%, 34%, and 39%.

Substantiation of the validity of the EHBF being about 30 ml/kg/min. in anesthetized animals, based upon comparison with results obtained by the thermostromuhr and collection techniques, is open to criticism. Schmidt ¶ said: "It is disappointing to have to admit that the thermostromuhr is unreliable quantitatively and is not even entirely dependable qualitatively. . . . The conclusion is inescapable that the only acceptable calibration of a thermostromuhr is one made under conditions that do not differ in any important respect from those under which the experimental observations were carried out." Reason for criticism of the collection technique has already been mentioned.

The value for splanchnic oxygen consumption obtained in this study, 2.5±0.72 ml/kg/min., which is dependent on hepatic blood flow and the peripheral arterial, hepatic vein oxygen difference, is in agreement with that reported by others.||

Sherlock [6] reported that in humans when the peripheral sulfobromophthalein sodium

|| References 40 and 41.

¶ Comment by C. F. Schmidt in discussion of thermostromuhr by D. E. Gregg.[44]

|| References 14 and 34.

level is less than 1 mg. per 100 cc., unusually high values for EHBF are obtained. In the dog, however, this has not been the experience of Casselman and Rappaport,[45] nor has it been ours. In the series of anesthetized animals the EHBF was found to be 48 ml/kg/min. in the seven animals where the peripheral sulfobromophthalein sodium level was less than 1 mg. per 100 cc. and 51 ml/kg/min. in the 13 which had a peripheral sulfobromophthalein sodium of more than 1 mg. per 100 cc. Likewise, no significant difference was found in the unanesthetized group.

In comparing the two groups—unanesthetized and pentobarbital anesthetized animals—Fisher's *t*-test was used. Only a statistical difference was found for oxygen consumption and cardiac index. The former had a *t* value of 5.7 with a *P* of 0.001 and the latter a *t* value of 3.0 with a *P* of 0.001.

Four unanesthetized animals displayed unusually high cardiac outputs. Three of these may be attributed to increased oxygen consumption as a result of restlessness due to the face mask. In the fourth a low peripheral arterial, mixed venous oxygen difference accounted for the increase in cardiac output. Although the mean cardiac index for these animals was almost double that of the other four, there was no proportionate increase in hepatic blood flow. From these observations it is suggested that increase of cardiac output in the unanesthetized animal during periods of excitement is not simultaneously followed by increased hepatic blood flow.

Our findings would indicate that ether anesthesia results in approximately a 40% increase in EHBF. As previously noted, this is not in agreement with the report of Pratt [16]; however, our findings are tenable when it is considered that Blalock [46] reported that ether anesthesia results in an increase of 76% in cardiac output and that the output of the heart is less than normal only when the depth of anesthesia is profound. It is unlikely that there would be a decrease in hepatic blood flow concomitant with such an increase in cardiac output.

Increasing evidence would indicate that the basic assumptions upon which the sulfobromophthalein sodium method is based are valid, and, therefore, this technique may be used for estimating hepatic blood flow. It has been demonstrated that no statistically significant difference exists between simultaneous measurements of portal vein and aortic dye concentrations.¶ Lorber and others [47] reported that the excretion of sulfobromophthalein sodium in the bile with subsequent intestinal reabsorption is of little consequence. On the basis of the evidence presented by Werner,[7] Pratt,[9] Casselman,[45] and others, the assumption that a sample of blood from one hepatic vein is representative of the entire hepatic outflow must be considered valid. The most controversial aspect of the method rests with the magnitude of extrahepatic removal of sulfobromophthalein sodium from the blood. Certainly, as Casselman has stated, quantitative information regarding sulfobromophthalein sodium removal, when obtained from hepatectomized, nephrectomized, eviscerated, or other surgically traumatized animals, cannot be applied to the normal dog. That there is a degree of extrahepatic sulfobromophthalein sodium removal in the normal animal under conditions of determination of blood flow sufficient to significantly alter the results still remains to be proved.

It is generally agreed that variations in normal hepatic blood flow are great and that any given measurement is only indicative of the flow at the time it is performed. Therefore, in the evaluation of experimental data dealing with hepatic blood flow, it is essential that a significant number of determinations be made to be compared with the normal under as closely similar conditions as possible. What constitutes normal hepatic flow in the anesthetized dog in all probability depends upon the state of anesthesia. It is this which most likely is the variable that has resulted in such a range of normal values reported in the literature.

¶ References 9 and 45.

SUMMARY AND CONCLUSIONS

In order to more critically evaluate the effect of certain experimental surgical procedures affecting the circulation of the liver, it is important to establish quantitatively what constitutes normal hepatic blood flow. A review of the literature concerning the use and results obtained by sulfobromophthalein sodium and other methods for estimation of hepatic blood flow in the dog has been presented. Reports of normal flows varying from 27.6 to 56 ml/kg/min. are probably a reflection of the state of anesthesia under which observations were made. In this laboratory no difference in estimated hepatic blood flow (EHBF) was found for animals either anesthetized with pentobarbital or in the unanesthetized state. Blood flow in the former group was 49 ± 7.4 mg/kg/min. and 46 ± 10.1 ml/kg/mm. in the latter. Because of the close agreement of these values with those obtained by others in unanesthetized animals, they probably represent the average value for the EHBF in the normal dog.

Hepatic blood flow increased during ether anesthesia, the mean value for 10 dogs being 70 ± 4.1 ml/kg/min. In the pentobarbital anesthetized animal simultaneous determination of cardiac output with EHBF demonstrated that hepatic blood flow constitutes 30% of the cardiac output. Greater variability in this relationship was found in the unanesthetized dog where marked increases in cardiac output due to restlessness resulted in no change in hepatic blood flow.

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Evaluation of Polyvinyl Pyrrolidone as a Plasma Expander

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Investigation of substances which will substitute for or expand the plasma component of the blood has been intensive in recent years. The need of such a substance which can be stockpiled is obvious in the disturbed society of today, with the prevalent threat of atomic warfare and its ability to produce thousands of civilian casualties in a few seconds. One of the plasma expanders is polyvidone (polyvinyl pyrrolidone), a substance synthesized from acetylene and ammonia by Weese and Hecht.[1] Polyvidone is currently produced under the trade name PVP-Macrose.* The present study is an attempt to evaluate polyvidone as a plasma expander.

As supplied by the manufacturer, polyvidone (PVP-Macrose) is an aqueous, straw-colored solution containing 3.5% polyvinyl pyrrolidone and small amounts of sodium chloride, potassium chloride, calcium chloride, magnesium chloride, and sodium bicarbonate. It has a pH range of 5.7 to 7.0, and its viscosity is twice that of water. The solution is by measurement slightly hypertonic, the osmotic pressure being 300 to 350 mm. of water, as compared with 250 to 300 mm. of water for serum. Polyvidone is supplied in flasks of 500 cc. for intravenous use. No toxic symptoms have followed the intravenous injection of polyvidone in cats, rabbits, mice, and monkeys, although dogs show a severe sensitivity which necessitates previous desensitization.[2] No toxic reactions are reported by the Germans to have occurred in the 500,000 military casualties in which it was used.

The present attempt to evaluate polyvidone as a plasma expander has been generally divided into three groups of studies. The first group represented an effort to determine whether the material remains in the intravascular compartment. If it does remain in that compartment, then hemodilution should occur and should be available for measurement by determination of the hematocrit value. The second group of studies attempted further to demonstrate whether the infused material remained in the plasma compartment by measuring the plasma volume and the total available fluid periodically after the administration of polyvidone. The third group represented clinical trials in patients who were hypotensive from hemorrhage in the interval prior to the arrival of blood or in instances where no blood was available.

In the first group of patients, the method of study was to determine a control hematocrit value prior to the intravenous injection of polyvidone. The patient was given 500 or 1000 cc. of polyvidone and then after infusion hematocrit samples were drawn periodically until the volume of packed cells had returned to preinfusion levels. Forty-two patients were studied in the first group. No fluid or electrolyte imbalance was present in any of these patients at the time of study. They were either in a preoperative status on unrestricted intake or at least a week had elapsed since operation and intake had been

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* The PVP-Macrose used in this study was supplied by Schenley Laboratories, Inc.

fully resumed. Thirty-eight patients received 1000 cc. of polyvidone by intravenous drip during a two-hour period. Two of these patients failed to receive the total amount, one receiving only 650 cc. and another 900 cc. The volumes of packed cells were determined from ½ to 2 hours, from 3 to 5 hours, and from 20 to 24 hours after the completion of the infusion. Occasionally, there were determinations made from 36 to 48 hours after the infusion when the hematocrit value had not returned to control levels prior to that time. Two patients in this group showed an unexplained rise in the hematocrit level after the injection of polyvidone. In the remaining 36 patients it will be noted in Figure 1 that the hematocrit level fell an average of 5.5 vol.% in the average case. At the end of 24 hours, the hematocrit value was within the normal daily range of 2 vol.%, except in seven instances in which hemodilution persisted 48 hours or longer. One patient showed a slight drop in the hematocrit level followed by a rise above the preinfusion level at 24 hours, but dehydration from withholding intake could not be excluded in this patient.

In the remaining 4 of the 42 patients in the first group, after a control hematocrit determination, 500 cc. of polyvidone was given by rapid intravenous injection within a period of 20 minutes. Hemodilution occurred in each case, averaging 3.5 vol.% decrease in the hematocrit level 4 hours after the completion of the injection, with a gradual rise to equal preinfusion determinations at the end of 24 hours. These results are shown in Figure 2.

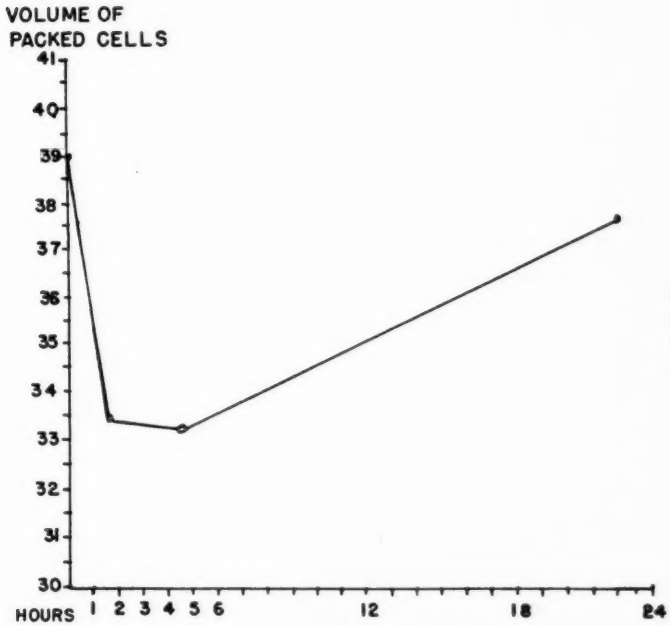

Fig. 1.—Average effect on the hematocrit value of the administration of 1000 cc. of polyvidone in two hours.

No local reaction occurred in any patient in this group, either from the injection site or from any site of extravasation. There was only one general reaction in this group. This patient had been burned 15 months prior to admission to this institution. Third degree burns were present on the anterior chest, abdomen, and thighs. He had received a total of 44 blood transfusions with a general reaction to each one. When polyvidone was injected into this patient, he experienced a chill and a rise in temperature which was

readily controlled by acetylsalicylic acid. No other symptoms of hypersensitivity were observed in this patient.

The second group of studies was concerned with the tracing of the injected polyvidone in the fluid compartment of the body available to measurement—the extracellular compartment, composed of the intravascular fluid and the interstitial fluid. The intravascular fluid, or plasma volume, was measured by the Evans blue dye method. The interstitial fluid was measured as total available fluid by the thiocyanate method. The first portion of this group of patients was studied by means of plasma volumes alone. These cases received Evans blue dye, injected for control determinations. Polyvidone was then given in amounts of 500 cc. by rapid intravenous injection in 20 minutes or 1000 cc. by slow intravenous injection during two hours. Evans blue dye measurement of the plasma volume was done from two to four hours after the infusion was completed. Fluids were not restricted during the study.

There were 11 patients studied by the Evans blue dye method alone. Four of the eleven cases were eliminated from the series owing to technical errors. These errors were chiefly the extravasation of indeterminate amounts of dye or of the infusion or both, rendering the results valueless. The determinations in the other seven cases can be seen in Table 1. It will be noted that there was a satisfactory expansion of the plasma volume representing a mean increase of approximately 50% of the infused polyvidone, except in two instances. The exceptions were two patients given 500 cc. by rapid injection who showed a rise in plasma volume beyond the amount of fluid given. This increase beyond the amount received probably can be explained by the rapid injection suddenly increasing the osmotic pressure of the plasma, resulting in a shift of fluid from the interstitial fluid space into the intravascular space.

TABLE 1.—*Plasma Volume Determinations with Infusion of Polyvidone*

Case	Polyvidone, Cc.	Plasma Volume, Cc.		
		Before Infusion	2 Hr. After Infusion	Change
1.....	1,000	2,483	3,054	+571
2.....	1,000	3,084	3,404	+320
3.....	1,000	2,406	2,926	+520
4.....	1,000	2,640	3,526	+886
5.....	500	2,328	3,024	+696
6.....	500	3,222	3,620	+398
7.....	500	2,082	2,627	+545

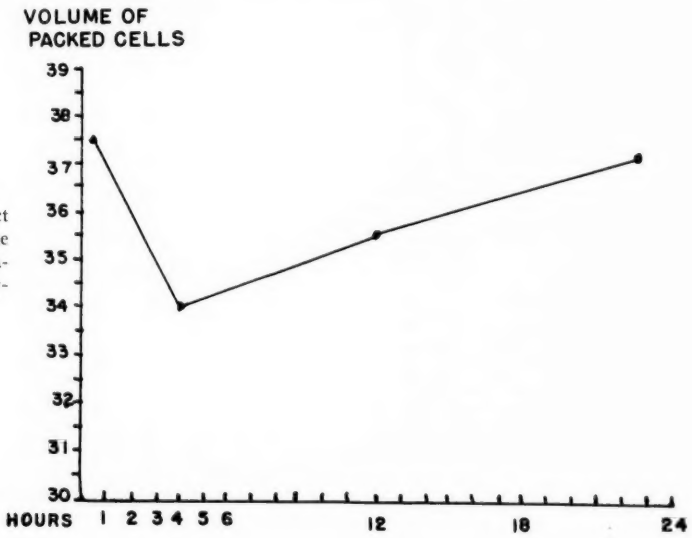

Fig. 2.—Average effect on the hematocrit value of the rapid administration of 500 cc. of polyvidone.

The second portion of the second group of patients was studied by means of Evans blue dye, to determine the plasma volume, and thiocyanate, to determine the total available fluid. The patients were allowed fluids as desired during the period of study. These cases were given Evans blue dye and thiocyanate for control determinations. One liter of polyvidone was then injected intravenously during a 2-hour period, except in one patient who received only 650 cc. Plasma volume and total available fluid were determined at 2 hours and again at 22 hours after the infusion was completed. Twenty cases were studied by this method, but five cases were discarded because of technical errors. In one further case the serum was cloudy, and the results was undoubtedly erroneous. The data in the 14 patients are presented in Table 2. The plasma volume determinations show an average rise in two hours of 500 to 600 cc. after a liter of polyvidone was administered, except in one case in which the increase was only 121 cc. These findings indicate that more than half of the polyvidone was present in the intravascular compartment two hours after the infusion. In the majority of the cases this hemodilution had almost returned to preinfusion levels at the end of 22 hours after infusion, although two cases showed a persistent rise of 500 to 800 cc. at 22 hours after the injection.

TABLE 2.—*Changes in the Plasma Volume Following Infusion of Polyvidone Without Restriction of Oral Fluids*

Case	Polyvidone, Cc.	Plasma Volume, Cc.			
		Before Infusion	2 Hr. After Infusion	24 Hr. After Infusion	Change at 2 Hr.
1.....	1,000	2,129	2,728	2,990	+599
2.....	1,000	3,139	3,644	3,116	+505
3.....	1,000	2,811	3,308	3,076	+497
4.....	1,000	3,011	3,185	2,953	+174
5.....	1,000	3,185	3,909	.....	+724
6.....	1,000	2,661	3,507	.....	+846
7.....	1,000	2,654	3,583	2,622	+929
8.....	1,000	2,529	3,076	3,208	+547
9.....	1,000	2,855	3,644	3,116	+789
10.....	1,000	2,425	2,884	.....	+459
11.....	1,000	2,797	2,918	.....	+121
12.....	1,000	2,209	2,887	.....	+678
13.....	575	3,346	4,132	.....	+786
14.....	1,000	2,009	2,544	2,087	+535

TABLE 3.—*Changes in Total Available Fluid Following Infusion of 1000 Cc. of Polyvidone Without Restriction of Oral Fluids*

Case	Total Available Fluid, Cc.			
	Before Infusion	2 Hr. After Infusion	24 Hr. After Infusion	Maximal Change
1.....	14,377	14,804	18,571	+ 427
2.....	20,053	26,000	19,359	+5,947
3.....	19,050	20,000	18,585	+ 950
4.....	18,585	19,359	19,050	+ 774
5.....	17,558	18,140	.....	+ 582
6.....	14,444	.....	15,000	+ 556
7.....	19,500	19,808	21,081	+ 308
8.....	15,600	24,355	17,721	+8,755
9.....	16,064	19,538	17,442	+3,474
10.....	14,519	17,721	.....	+3,202
11.....	12,583	18,050	.....	+5,467
12.....	18,140	24,000	.....	+5,860
13.....	19,868	20,595	.....	+ 727
14.....	13,607	18,571	14,377	+5,964

Fourteen patients in the second group had determinations of the total available fluid by the thiocyanate method. The results in this group of patients are shown in Table 3. The total available fluid determinations have been of considerable interest. An average rise of 2935 cc. occurred in the total available fluid in these 14 patients after they received 1000 cc. of the solution. The reason for the enormous rises, varying from 300 cc. to almost 9000 cc., is not known. As shown in Table 2, the average plasma volume rise after a liter of polyvidone was 585 cc. If this figure is subtracted from the average rise in total available fluid, the result indicates that the increase in body fluid occurs principally in the interstitial fluid and averages 2350 cc. at two hours after administration of 1000 cc. of the plasma expander. It may be speculated that the polyvidone not found present in the plasma after infusion (400 to 500 cc. on the average) is escaping into the interstitial fluid space, where an increase in osmotic pressure occurs, causing an internal fluid shift from the intracellular space. Another possible source of fluid for the increase in the interstitial fluid is liquid ingested during the infusion and during the two hours after completion of the infusion. The slight cellular dehydration which may result from the probable shift of intracellular fluid into the extravascular space has not been shown to have any deleterious effect that is clinically detectable.

In order to eliminate this second possible source of fluid for the increase in interstitial fluid, six patients were not allowed to take fluids from the time of the determination of the control plasma volume and total available fluid until after the determinations were repeated two hours subsequent to the completion of the injection of 1000 cc. of polyvidone. These six cases showed an average plasma volume increase of 505 cc. two hours after the infusion. In comparison, the patients on unrestricted fluid intake demonstrated an average increase of 585 cc. in plasma volume. The average rise in total available fluid was 1458 cc., as contrasted to 2935 cc. in the patients without curtailment of liquids during the test. These six cases were allowed to ingest unlimited fluid after the two-hour post-infusion blood samples were obtained. Evans blue dye and thiocyanate were then repeated at 22 hours after the injection. The average case showed at that time a rise in total available fluid of 2792 cc. These figures indicate that probably both mechanisms have a part in the total available fluid increase. In the absence of fluid intake, the available fluid increase was 1458 cc. with the injection of 1000 cc. of polyvidone. There may be a shift of approximately 500 cc. of fluid from the intracellular space, not considering the urinary and insensible loss during the four hours of the experiment. However, if the patient is allowed fluids as he desires during the interval of the study, then the total available fluid increase doubles in volume, on the basis of retention of the ingested fluid in the extracellular space.

The third group of studies was concerned with the clinical effect of the injection of polyvidone into hypotensive patients. These patients represented acute surgical emergencies who were usually hypotensive from loss of blood volume. Polyvidone was given as supportive treatment during the time interval required for the matching and cross matching of blood for transfusions or in those instances where blood of the patient's type was either not available or not readily procurable. The solution was usually given by rapid infusion during a 15- to 20-minute period. The amount of solution injected usually was 500 to 1000 cc., although as much as 2000 cc. of polyvidone has been given to a patient in a 45-minute period. Twenty-four patients have received polyvidone in the treatment of hypotension. Eleven of these patients received the infusion in the emergency room. Ten were supported with the solution during or immediately after an operative procedure, and three patients who were moribund received polyvidone as part of desperate resuscitative efforts. Blood transfusions, if available, were not withheld unless the hypotension was completely relieved by the infusion and remained stabilized in the absence of continuing loss of blood volume. Twelve of the twenty-four patients did not receive transfusion after the injection of polyvidone. Nine patients received blood after the infusion, and three patients died before a blood transfusion could be begun. A satisfactory response to polyvidone was recorded where the blood pressure did not fall to lower levels in the presence of continuing blood loss and

TABLE 4.—*Changes in the Plasma Volume and Total Available Fluid with Restriction of Oral Fluids*

	Plasma Volume, Cc.					Total Available Fluid, Cc.			
Case	Expected	Before Polyvidone Infusion	2 Hr. After Polyvidone Infusion	22 Hr. After Polyvidone Infusion	Maximal Change	Before Polyvidone Infusion	2 Hr. After Polyvidone Infusion	22 Hr. After Polyvidone Infusion	Maximal Change
1.....	2025	1723	2280	1807	+557	.....	.....	.....	.....
2.....	3375	3258	3525	3496	+267	21,071	21,781	22,206	+1,135
3.....	4095	3785	4257	3720	+472	24,581	25,500	24,581	+ 919
4.....	3150	2836	....	2981	+145	17,356	20,000	19,359	+2,644
5.....	3150	3554	4232	4057	+678	25,167	.....	31,750	+6,583
6.....	2160	1903	2443	2183	+543	13,855	15,408	1,600	+2,145

where the blood pressure was elevated in those instances where blood loss had ceased. Twenty patients showed a satisfactory response to the infusion. Pulmonary edema developed in one patient, a 64-year-old Negro man who received 500 cc. of the solution in 15 minutes in the treatment of hypotension immediately after an operative procedure. The pulmonary edema was easily controlled with intravenous aminophylline. Whether the pulmonary edema resulted from circulatory overloading in a patient with poor cardiac reserve or from the escape of the polyvidone from the pulmonary capillaries, with local increase in extracellular osmotic pressure and an internal fluid shift, was not determined. Three terminal cases were not benefited from the injection of polyvidone and death ensued from myocardial infarction, pulmonary embolism, and cerebrovascular accident in one instance each. Cases representative of the effect of polyvidone in these hypotensive patients follow.

REPORT OF CASES

CASE 2.—This patient received 500 cc. of blood during débridement of extensive burn slough of the left leg. Blood pressure fell to 84/60 at completion. The patient received 1000 cc. of polyvidone, with a rise in blood pressure to 140/90 in a two-hour period. No blood transfusion was given.

CASE 3.—This patient was admitted with massive upper gastrointestinal bleeding. Blood pressure was unobtainable. He received 1000 cc. of polyvidone in 40 minutes, with a rise in blood pressure to 94/56. Blood transfusion was begun.

CASE 7.—During fragmentation of an intrathoracic extension of a nodular goiter, the patient's blood pressure became unobtainable. She received 2000 cc. of polyvidone in 45 minutes. Blood pressure had risen to 90/60 when a blood transfusion was begun.

CASE 9.—This woman was admitted with diagnosis of ruptured uterus. She was given 1000 cc. of polyvidone while blood was being matched. Blood pressure was recorded as 112/70 and did not fall during the hour that the patient received the polyvidone. Steady bleeding from the uterus was found at laparotomy.

CASE 22.—This patient had an uneventful course for three days after a radical neck dissection for carcinoma of the lip. The blood pressure suddenly became very low and then unobtainable. Polyvidone, 1000 cc., was given without effect, and the patient died before a blood transfusion could be begun. Death was believed to be due to a cerebrovascular accident.

SUMMARY AND CONCLUSIONS

The intravenous injection of polyvidone causes an expansion of the plasma volume which disappears in 20 to 24 hours in the average case.

The hematocrit value fell an average of 5.8 vol.% 3 to 5 hours after an infusion of 1000 cc., with a gradual return to the normal daily range of $\pm$ 2 vol.% at the end of 24 hours, although hemodilution persisted in 20% of the patients for 48 hours or longer.

The plasma volume showed a mean increase of one-half of the amount of polyvidone, given, as determined by the Evans blue dye method.

The total available fluid, as measured by the thiocyanate method, showed an average rise of three times the amount of polyvidone infused.

It is suggested that increase in total available fluid beyond the amount of polyvidone given is due to the retention of ingested fluid and an internal fluid shift from the intracellular space.

No local reactions were observed. One instance of chill and one instance of pulmonary edema from too rapid administration were the only constitutional reactions noted.

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The Chronic Subluxating Ankle

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It has been shown that a significant percentage of patients who "sprain" their ankle sustain a permanent disability.* In fact, Hughes has shown that in 57 cases of injury to the ankle without bony damage about 50% of the patients showed some tilting of the talus when roentgenograms were made with the ankle in forced inversion. Most authors † state that tears of the fibular collateral ligament of the ankle severe enough to be demonstrable roentgenologically in forced inversion should be treated in plaster for 6 to 10 weeks. If the injury to the ligaments is extensive (complete tear of the anterior talofibular and calcaneofibular ligaments), it has been suggested that the ligament be repaired primarily.[5]

There is a group of patients who eventually have chronic subluxating ankles. Some few patients who sustain severe ligamentous injuries may have to be classed in this group, in spite of proper immobilization in plaster at the time of injury, but the great majority are patients who originally were inadequately treated. Because of excellent results obtained by the Watson-Jones reconstruction of the lateral ligament of the ankle, and because reports on this procedure are so few, we have prepared a report on seven patients for whom this operation was carried out at the Mayo Clinic between January, 1950, and April, 1954. The condition of all has been followed for at least a year postoperatively, the average being 20 months. Ages ranged from 18 to 56 years; most patients were young adults.

The average duration of symptoms in this group of patients was seven years. All but one gave a definite history of a sprain as initiating the symptoms. The original injury in each case was treated lightly, and the patients reported subsequent "sprains" of the ankle. Intermittent pain in the ankle and a sense of insecurity in the ankle, associated with swelling below the lateral malleolus, were the commonest complaints. Several patients previously had been told that they had arthritis of the ankle.

The anatomic aspects of these injuries to the lateral ligaments of the ankle are in dispute. There are three main components of the fibular collateral ligament: (1) the anterior talofibular ligament, (2) the calcaneofibular ligament, and (3) the posterior talofibular ligament (Fig. 1). The lateral capsule lies between the first two ligaments named. Recent writers ‡ have emphasized the importance of the anterior talofibular ligament, because, clinically, sprains do occur in plantar flexion when this ligament is taut. Severing this ligament alone in cadavers, according to Anderson and Lecocq,[5] will result in a tendency toward a slight anterior subluxation of the joint, and, if the lateral capsule is also severed, about 7 degrees of tilting of the talus is permitted when the foot is in equinus. This ligament is the one most commonly involved in a sprain. Most writers believe that the lateral calcaneofibular ligament is the most important in producing marked subluxation of

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* References 1 and 2.

† References 3 and 4.

‡ References 3-6.

Fig. 1.—The three components of the fibular collateral ligament of the ankle.

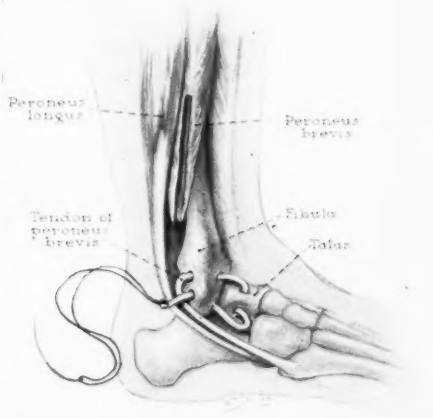
the ankle; however, studies on cadavers in which this ligament alone is severed show only a slight degree of tilting. Perhaps the injury which most commonly produces the greatest instability in an ankle is an injury to the anterior talofibular ligament and the calcaneofibular ligament. The posterior talofibular joint is seldom of clinical importance.

When roentgenograms are made to show subluxation of the talus on the tibia, it is best to take the anteroposterior views with the foot in slight equinus, in order to demonstrate laxity of the anterior talofibular ligament. The foot of the patient should be firmly grasped at the calcaneus and held in inversion. Bonnin [2] has demonstrated that there is a condition which he calls "hypermobile hind feet" and that 5% of the population without previous history of injury to the ankle will show some degree of this condition bilaterally. In a high percentage of patients, and especially in males, the talus is seen roentgenologically to be tilted. A high percentage of patients with severe sprains have hypermobile hindfeet. Approximately 5% of the population will show some degree of tilting of the talus unilaterally and will give a history of previous sprains. Therefore, it is important to include both ankles when roentgenograms are made of the ankles in inversion. This measure may rule out a congenital hypermobile foot. Moreover, it is also important to obtain a history of previous injuries to the ankles before a patient is subjected to a long period in a cast in what may be an erroneous assumption that the injury at hand is the initial injury to the lateral ligament.

The treatment may be surgical or conservative. Conservatively, use of a wide heel or an outer-heel wedge, and exercises for the peroneal muscles are of value. In some cases patients are given short leg braces, with an outer T-strap to prevent inversion.

The best surgical treatment of this condition is reconstruction of the fibular collateral ligament according to the method of Watson-Jones.[7] This method utilizes the peroneus brevis tendon, which is severed from its muscular origin and is run through a ¼-in. drill hole in the fibula and through a drill hole in the talus at the level of the sinus tarsi and then back through a drill hole in the fibula, at which point the tendon is attached to itself. The tendon is not always long enough to permit its being run back through the second drill hole in the fibula. Figure 2 illustrates the method. The tendon should not be

Fig. 2.—The Watson-Jones reconstruction of the fibular collateral ligament in which the tendon of the peroneus brevis is used for linking.



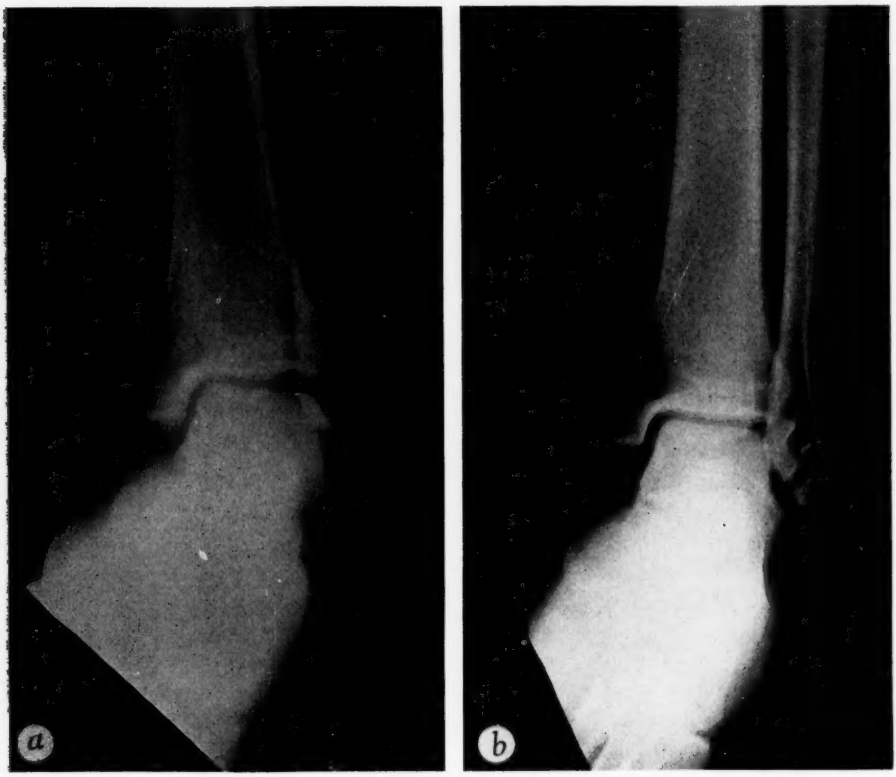


Fig. 3.—(*a*) Preoperative roentgenogram of an ankle in forced inversion, showing partial disruption of the fibular collateral ligament. (*b*) Postoperative roentgenogram of the same ankle as that in (*a*) in forced inversion. This roentgenogram was taken one year after performance of the Watson-Jones reconstruction of the lateral ligament, and it shows the absence of tilting of the talus.

stripped out of its sheath and retinaculum below the medial malleolus. The advantage of this procedure is the fact that it restores the important anterior talofibular ligament by means of a tendon which is not likely to stretch. Figure 3 (*a*) shows the preoperative roentgenograms of a tilting talus, and Figure 3 (*b*) shows the same ankle one year later in forced inversion (note the absence of tilting).

We have followed the condition of seven treated patients; six of them have obtained an ankle that is stable and free of pain and swelling, without excessive limitation of motion. In one case the result is fair; it no doubt would have been better had not osteoarthritis of the ankle been present preoperatively. The possible development of such a complication is one reason for the need of repairing such ankles early. In three cases the peroneus brevis tendon was not long enough to permit the maneuver described above. This problem was solved in one case by splitting the tendon, in another by use of a split segment of the peroneus longus tendon, and in a third by not drawing the peroneus brevis tendon back through a second drill hole in the fibula.

Others § have reported excellent results from this procedure. In fact, very few failures have been reported.

§ References 4, 5, and 8.

SUMMARY

The Watson-Jones reconstruction of the fibular collateral ligament of the ankle, described and illustrated in this paper, has been a very successful operation in our hands for treatment of the chronic subluxating ankle.

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Myocardial Infarction Associated with Surgical Operation

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INTRODUCTION

Many reports have appeared stressing the frequency of the association of surgical procedures and acute myocardial infarction in poor-risk patients, especially those more than 50 years of age.* The fall in blood pressure which often accompanies, or follows, the administration of an anesthetic and the performance of surgery has been considered a significant factor in the reduction of blood flow to the myocardium and the occurrence of coronary arterial thrombosis.† Anemia may be an added factor in decreasing the amount of oxygen available to the heart. Coronary arterial sclerosis with narrowing of the arterial lumina, often unsuspected, is of obvious primary importance, for pathologic observations have revealed that severe coronary arteriosclerosis is almost always present in patients with myocardial infarction discovered postoperatively.[8] The clinical diagnosis of myocardial infarction can be difficult,[3] especially if it occurs during anesthesia or in the immediate postoperative period when the patient's sensorium is clouded. However, most reports have been based on clinical studies. The present study of autopsied patients was undertaken in an effort to further define the role of surgical procedures and anesthetics in the development of acute myocardial infarction.

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From the Department of Pathology, Washington University School of Medicine.

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† References 7-9.

MATERIAL AND METHODS

The autopsy files of the Department of Pathology at Washington University for the period 1942 through 1954 were examined. A total of 4453 adult Barnes Hospital patients were autopsied during this period. The clinical records of Barnes Hospital were made available by the Departments of Medicine and Surgery.

Acute Myocardial Infarction.—An anatomical diagnosis of acute myocardial infarction was made on 386 of these 4453 patients. From autopsy protocols of these 386 patients data were obtained concerning their age, sex, heart weight, and extent of arteriosclerosis and luminal narrowing of the coronary arteries, and the presence of a fresh thrombus occluding a coronary artery. The clinical records of the 386 patients with an anatomical diagnosis of acute myocardial infarction were carefully studied, and data were derived pertaining to the history of anginal pain prior to the present illness, the blood hemoglobin value, and the history of a recent surgical operation performed during the final admission.

Acute Myocardial Infarction and Surgical Operation.—Fifty of the patients with acute myocardial infarction had had a surgical operation within one month of death. From clinical records of these patients data were obtained concerning the type of operation, anesthetics used, blood pressure fluctuations during the operative and immediate postoperative periods, and the time of operation in days before death.

Postoperative Death with Autopsy.—During this same period (1942-1954) there were 1157 autopsies performed in this department on patients who had died within one month after surgery. From the autopsy protocols of these patients data were obtained concerning age, sex, type of operation, and the postoperative day on which death occurred.

Comparative Data Derived from Clinical Records.—Clinical records of Barnes Hospital for the peri-

ods 1942-1945 and 1947-1953 inclusive have been coded in an International Business Machine Diagnostic and Operative Index Book (I. B. M. book).[10] This, in part, determined our selection of the time period for this study, for comparative data could be derived from the coded I. B. M. book for approximately the same period during which the autopsies were performed. From this I. B. M. book data were obtained concerning the frequency of the clinical diagnosis of acute myocardial infarction and also the number of clinical diagnoses of acute myocardial infarction in patients having surgery during the same hospital admission. The age and sex of these patients and the type of operations performed were also obtained.

In addition, data concerning the total number and types of operations performed and the frequency with which the various types of anesthetics were used at Barnes Hospital during the same period were obtained from the departments of surgery and anesthesiology.

RESULTS

The incidence of acute myocardial infarction in 4453 adult Barnes Hospital patients autopsied from 1942 through 1954 was 8.7% (386 patients). Fifty (13%) of the autopsied patients with acute myocardial infarction had had a surgical operation during the final admission and within one month of death (average, seven days).

Comparison of Autopsy and Clinical Data on the Nonpostoperative and Postoperative Patients with Acute Myocardial Infarction

(Table 1) Of the nonpostoperative patients with acute myocardial infarction 66% were men and 34% women. This is approximately the same sex distribution as is found in our entire adult autopsy series.[11] Of the postoperative patients with acute myocardial infarction 74% were men and 26% women. The average ages of the patients in the two groups (nonpostoperative and postoperative) were 62 and 67 years, respectively. The average weights of the hearts of the patients in the two groups were 515 and 489 gm., respectively. A fresh thrombus occluding the lumen of a coronary artery was found at autopsy in 127 (38%) of the 336 nonpostoperative and 15 (30%) of the 50 postoperative patients with acute myocardial infarction. At least "moderate" arteriosclerosis of the coronary arteries was described in the autopsy protocols of all of the patients with acute myocardial infarction. Marked narrowing or complete occlusion of the lumen of one of the coronary arteries was not described in the autopsy protocols in 44 (13%) of the nonpostoperative and 7 (14%) of the postoperative patients with acute myocardial infarction. A history of anginal pain experienced prior to the patient's present illness was described by approximately one half of the patients in both groups. In addition to the recent infarct, a healed myocardial infarct was found at autopsy in 31% and 42% of the patients in each group respectively. The admission blood hemoglobin value was available in 252 nonpostoperative and 43 postoperative patients with acute myocardial infarction. The average blood hemoglobin value in these two groups was similar, 13.3 and 12.2 gm. per

Table 1.—*Comparison of Autopsy with Clinical Data on the Nonpostoperative and Postoperative Patients with the Anatomic Diagnosis of Acute Myocardial Infarction*

Group	No. of Cases	Sex	Av. Age, Yr.	Av. Weight of Heart, Gm.	Presence of Fresh Thrombi in Coronary Artery	Absence of Marked Narrowing of Coronary Artery	History of Angina	Presence of Healed Infarct	Av. Blood Hemoglobin Value, Gm.	Blood Hemoglobin Below 8 Gm.
Nonpostoperative patients	336	M 226 (66%) F 114 (34%)	62	515	38%	13%	50%	41%	13.3	5%
Postoperative patients	50	M 37 (74%) F 13 (26%)	67	489	30%	14%	48%	42%	12.2	5%

100 cc. respectively. The blood hemoglobin values were below 8 gm. per 100 cc. in 11 (5%) and 2 (5%) of the patients in the two groups, respectively.

Comparison of Autopsy and Clinical Data on Postoperative Patients With and Without Acute Myocardial Infarction

From 1942 through 1954 there were 227,649 surgical operations performed at Barnes Hospital, of which approximately 45% were major operations. During this period 1157 autopsies were performed on adult patients who died within one month after a surgical operation. Fifty (4.3%) of them had an acute myocardial infarct. The average age of these patients without acute myocardial infarction was 55 years, and with acute myocardial infarction 67 years. The 1157 patients were divided into nine groups according to the type of operation which was performed and the average age of the patients in each group, with and without acute myocardial infarction, was determined. These data are summarized in Table 2. Most (90%) of the postoperative patients with acute myocardial infarction had undergone "major" surgical procedures.

Table 2.—*Type of Operation Performed on Postoperative Patients With and Without Acute Myocardial Infarction Autopsied from 1942 Through 1954*

Type of Operation	Autopsied Postoperative Patients Without Infarcts		Autopsied Postoperative Patients With Infarcts	
	No. of Cases	Av. Age, Yr.	No. of Cases	Av. Age, Yr.
Craniotomy	231	47	2	48
Thoracotomy	244	51	5	58
Laparotomy	460	60	11	71
Amputation	13	65	13	69
Radical neck dissection	26	61	4	63
Transurethral prostatectomy	38	72	3	68
Reduction of fracture	16	74	2	80
Ophthalmic	2	67	2	69
Miscellaneous	76	56	9	66
Total	1,107	55	50	67

Comparison of the Anesthetics Used at Barnes Hospital with the Anesthetics Administered to the Patients with Acute Myocardial Infarction Postoperatively

The records of the department of anesthesiology from 1942 through 1948 were available, and from these the frequency with which the various types of anesthesia were used was calculated. From the clinical records of the 50 postoperative patients with acute myocardial infarction, the various types of anesthesia administered to these patients were also determined. A rather high percentage of the patients who had acute myocardial infarction postoperatively had been given spinal anesthetics (30%), whereas spinal anesthetics comprised only 1.3% of the total anesthetics administered at Barnes Hospital. Otherwise, approximately the same percentages of the patients with acute myocardial infarction received the various anesthetics as did all other surgical patients.

Comparative Data on the Frequency and Accuracy of the Clinical Diagnosis of Acute Myocardial Infarction in Patients Who Had Had Recent Surgical Procedures

The I. B. M. Index Book in which the clinical diagnoses made at Barnes Hospital are coded was examined. These diagnoses were available for the years 1942 to 1945 and 1947 to 1953, inclusive. The first four clinical diagnoses on each patient are indexed. During these 11 years the clinical diagnosis of acute myocardial infarction was made on 131 patients who also had a coded diagnosis of a significant surgical procedure. Such procedures as lumbar puncture, paracentesis, and blood transfusion, though indexed, were not considered significant. Of these 131 patients, 33 were autopsied and an anatomical diagnosis of acute myocardial infarction was made in 16 (48%). A clinical diagnosis of myocardial infarction was made in 21 (42%) of the 50 postoperative patients with an anatomical diagnosis of acute myocardial infarction. This calculation of the accuracy of clinical diagnosis was obtained by a careful study of the clinical and autopsy records of these 50 patients.

Blood Pressure Fluctuation During the Operative Period.—Half of the 50 postoperative patients with acute myocardial infarction had a preoperative blood pressure recorded as higher than 150 mm. Hg systolic and/or 90 diastolic. A fall in systolic blood pressure of 50 mm. Hg or more was recorded during the operative procedure in 20 (80%) of these 25 patients with hypertension and in 11 (44%) of the 25 patients without hypertension. Thirty-one (62%) of all 50 patients had a fall in systolic blood pressure of 50 mm. Hg or more, and in 16 patients this fall was more than 100 mm. Hg. In 11 of the 15 patients who received spinal anesthetics there was a fall of 50 mm. Hg or more in the systolic blood pressure.

COMMENT

Thirteen per cent of Barnes Hospital patients who were discovered at autopsy to have an acute myocardial infarct had had a recent surgical operation. From autopsy and clinical records we were unable to demonstrate any appreciable differences between a group of 50 postoperative patients and a group of 336 nonpostoperative patients with acute myocardial infarction.

Evidence of Preexisting Coronary Artery Disease.—Marked narrowing of the lumen of a coronary artery, healed infarcts, and a history of angina were equally common in the patients in either group, indicating that coronary artery disease was of equal importance in the production of acute myocardial infarction in all patients. The average heart weight was no greater and severe anemia was no more frequently present in the postoperative patients with acute myocardial infarction than the nonpostoperative patients with acute myocardial infarction, indicating that the requirements of the myocardium and the oxygen-carrying capacity of the blood were essentially the same in the two groups of patients. However, in isolated cases of both groups a hypertrophied myocardium, severe anemia, or both may have influenced the development of acute myocardial infarction.

Frequency of Thrombotic Occlusion of a Coronary Artery.—Theoretically, occlusion of a coronary artery by a thrombus is not always necessary for the production of a myocardial infarct. A patient with severely narrowed coronary arterial lumina during a period of hypotension, such as sometimes occurs with anesthesia or acute hemorrhage, might develop a myocardial infarct due to relative but not absolute lack of blood supply to an area of myocardium. However, recent coronary arterial thrombi were found as frequently in the nonpostoperative as in the postoperative patients with acute myocardial infarction. If any factors other than thrombotic occlusion of the coronary arteries precipitate the development of myocardial infarction, then such factors, not necessarily the same factors, must be as commonly operative among all patients with acute myocardial infarction as among the postoperative patients with acute myocardial infarction.

Hypotension.—A fall in systolic blood pressure of 50 mm. Hg or more was recorded during the operative period in 31 (62%) of the 50 postoperative patients with an anatomic diagnosis of acute myocardial infarction. A fall in blood pressure was more likely if the patient had hypertension before the operation. Undoubtedly, a drop in blood pressure could reduce coronary arterial blood flow, but we were unable to secure a group of comparable surgical patients by which the significance of this degree of hypotension could be evaluated.

Age.—The average age of the postoperative patients with acute myocardial infarction demonstrated at autopsy was 67 years as compared with an average age of 55 years for the postoperative patients without acute myocardial infarction who were autopsied during the same period. Postoperative patients with a clinical diagnosis of acute myocardial infarction had an average age of 63 years. This age difference between postoperative patients with and without myocardial infarction indicates that the likelihood of occurrence of acute myocardial infarction

during or after a surgical operation is greater in the older age group, although old age per se is not necessarily a factor in the development of a myocardial infarct.

Anesthetics.—Proportionately, spinal anesthetics were administered more frequently to the postoperative patients with acute myocardial infarction than to the entire group of patients undergoing surgery at Barnes Hospital. Other types of anesthetics were used with similar frequency in these two groups of patients. The selection of anesthetic to be used on older poor-risk patients may be responsible for the greater percentage of patients with acute myocardial infarction receiving spinal anesthetics.

Type of Operation.—In this series acute myocardial infarction was more frequently associated with amputation of the lower extremities than with any other surgical procedure. Half of the autopsied patients who died within one month after amputation had a recent myocardial infarct. It is not surprising that acute myocardial infarction is so common among these patients. All the amputations were performed because of the presence of severe arteriosclerotic peripheral vascular disease with slowly progressive gangrene. In none of the patients was an acute myocardial infarct suspected clinically prior to the amputation.

Accuracy of Diagnosis.—The complicated clinical picture often prevailing in the postoperative patient, especially the lowered sensorium, makes the diagnosis of acute myocardial infarction difficult.[3] The truth of this statement is supported by our data derived from clinical and autopsy records. The diagnosis of acute myocardial infarction was correct in approximately half of the postoperative patients in our series. In 58% of the postoperative patients in whom an acute myocardial infarct was demonstrated at autopsy, the infarct had not been diagnosed during life. Conversely, in half of the autopsied postoperative patients with a clinical diagnosis of acute myocardial infarction, no infarct was demonstrated at autopsy.

SUMMARY

A surgical procedure had been performed within the month prior to death in 50 out of a consecutive series of 386 patients with an anatomical diagnosis of acute myocardial infarction. Anatomic evidence of preexisting severe coronary artery disease, coronary arterial thrombi, severe anemia, and a clinical history of angina are present with similar frequency in the postoperative and nonpostoperative patients with acute myocardial infarction. The average age of the postoperative patients with acute myocardial infarction is 67 years, considerably greater than in autopsied postoperative patients who died of other causes. In the autopsy series from 1942 through 1954 there are 1157 autopsied patients who died within one month postoperatively; only 50 (4.3%) of these patients had an acute myocardial infarct demonstrated at autopsy. During this period 227,649 operations were performed at Barnes Hospital.

A fall in systolic blood pressure of 50 mm. Hg or more was recorded during the operation in 31 of the 50 postoperative patients with acute myocardial infarction. Proportionately, spinal anesthetics were administered more frequently to the postoperative patients with acute myocardial infarction than to the entire group of surgical patients at this institution, but no conclusion can be drawn from this fact because the selection of anesthetic to be used on these older, poor-risk patients may have accounted for the disproportionately large number receiving spinal anesthetics.

Half of the autopsied postamputation patients had a recent myocardial infarct.

The accuracy of the clinical diagnosis of acute myocardial infarction in postoperative patients in this series is approximately 50%.

Dr. Barry Wood Jr. suggested the original topic for investigation in this study, and Dr. Carl Moyer discussed the many problems involved.

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Multiple Primary Malignancies

A Case Report of Four in Succession

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To the surgeons who steadily spend thought, time, and a great deal of energy trying to eradicate cancer, it is truly encouraging to know that a patient with four primary successive major malignancies over a 21-year period was cured of three of them and survived the fourth by 7 years. With more than five years passing after the last cancer operation, it was hoped that surgery had once more triumphed, but such was not the case. It is believed, however, that a report of this nature will help sustain the continuing attack on this distressing disease, since, as the life span of our population becomes greater, surgeons may expect to be confronted with an increasing incidence of a cured first cancer and the subsequent development of a second, third, or even a fourth primary tumor. A brief review of this rare and interesting case is presented and added to similar ones found in the literature. Some particular aspects of multiple malignancies are considered.

REPORT OF CASE

A housewife aged 64 had always taken care of her health, had gone to her doctor when she felt that something was wrong, and had received excellent medical care. The record of her malignancies is as follows.

1. November, 1927, age 38. Carcinoma of the right breast. Radical mastectomy done for undifferentiated-cell carcinoma of the comedo type. No metastases identified in regional lymph nodes.

2. March, 1940, age 51. Carcinoma of the right ovary. Hysterectomy with bilateral salpingectomy and oophorectomy for papillary cystadenoma of the right ovary with malignant degeneration.

3. July, 1947, age 58. Carcinoma of the sigmoid colon. Resection of distal two-thirds of sigmoid and upper rectum with end-to-end anastomosis for adenocarcinoma, Grade 2. No metastases found in sigmoid mesenteric or periaortic lymph nodes. No evidence of carcinoma in liver or in pelvis from this tumor or previous ovarian malignancy.

4. May, 1948, age 59. Carcinoma of the left breast. Left radical mastectomy for adenocarcinoma, Grade 3, duct-cell type. No metastases to regional lymph nodes identified.

In May, 1949, a laparotomy was done for intestinal obstruction due to adhesions, and no abdominal carcinoma was evident. In the spring of 1954 the patient was quite well but by midsummer showed signs of pulmonary and liver metastases. At autopsy the lungs, liver, and retroperitoneal lymph nodes were extensively infiltrated with duct-cell sclerosing carcinoma similar to that of the fourth malignancy from the breast. Thirteen years elapsed between the first and second malignancies, whereas the last two were in rapid succession. With 21 years between the two breast tumors, there is no doubt that the second one was another primary. It also was of a different histologic type from the 1927 lesion.

Table 1 lists four other cases * from the literature of four metachronous (successive) primary malignancies along with our case. A very few of the tumors were relatively minor in character, but each one was an additional cross of anxiety for the patient to bear and certainly a challenge for the surgeon to support the patient mentally and defeat the cancer process. It is interesting to note that all these patients were women; four of the five had a breast cancer, and in each case it was the first cancer discovered.

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* References 1, 2, 3, and 4.

Two had both breasts involved; four had a cancer of one of the female sex organs, labia, cervix, uterus, or ovaries. All had a carcinoma of the colon or rectum, and all had three or more organs involved, a very rare occurrence. This frequency of a few locations might seem unusual, but it actually mirrors the commonest sites of malignancy in women and emphasizes those locations where tumors should be particularly looked for in the female.

CRITERIA OF INDEPENDENCY

From time to time criteria have been presented to establish or rule out the independence of multiple growths. Billroth, in 1869, formulated the requirements that each tumor must have an independent histologic primary appearance, the tumors must arise in different situations, and each tumor must produce its own metastasis. The suggestions of Goetze are perhaps more reasonable. He believed that tumors must have the macroscopic and microscopic appearance of the usual carcinoma of the organs involved, the exclusion of metastasis must be certain, and the diagnosis in each case may be confirmed by the character of the individual metastasis. The broader standards of Warren and Gates [5] seem more logical—namely, each tumor must present a definite picture of malignancy, each must be distinct, and the probability of one's being a metastasis of the other must be excluded.

INCIDENCE

The great majority of multiple neoplasms have been found at necropsy, and the postulates for distinguishing multiple primary malignant tumors from recurrent or metastatic processes have been established from autopsy rather than clinical findings. In the majority of these cases the tumors were considered to have occurred simultaneously. Data on the incidence of asynchronous, or metachronous, multiple primary malignant lesions are less satisfactory, and for the most part have been collected from clinical material. Much difficulty has been encountered in the selection of cases, and in some series lesions have been included which have been excluded in others. For example, patients who had survived the removal of one ovary and subsequently had a malignant neoplasm in the other ovary have been excluded from some series because of the frequency of metastasis from one side to the other.

Based on postmortem findings, the incidence of carcinoma at the Wisconsin General Hospital, the University of Michigan Hospital, and the Mayo Clinic [6] averaged about 30% of all autopsies.

Warren and Gates [5] reviewed the literature on multiple malignancies, largely autopsy reports, and found 546 multiple out of 29,740 total lesions, or an incidence of 1.84%. Of these cases, 28 had four or more foci, including the commonest sites of the skin and gastrointestinal tract. In their own series of 1078 cancer autopsies the multiple frequency was found to be 3.7%.

AVERAGE AGE AND HEREDITY FACTOR

Barrett and co-workers,[7] in a survey of 36 cases of multiple primary malignant neoplasms, found the average age at the time of appearance of the initial primary tumor to be 52.0 years, and the average time interval between primary tumors was 3.22 years. There were 32 women and 4 men in this series, a ratio of 8 to 1. The time interval between lesions was greatest in those confined to the gastrointestinal system and shortest in those involving the ovaries and gastrointestinal tract. The average age for Warren and Gates'[5] 1279 cases of multiple malignancies was 55.5 years, whereas for those with more than two primary cancers it was 54.0 years. In Warren and Ehrenreichs'[8] series of 194 patients with multiple malignancies there were 131 men and 63 women. The average age of the male group was 65.2 years, of the female group 56.9 years, and of the entire group 62.5 years.

Heredity may well play a part in the occurrence of multiple tumors. For Hurt and Broders [9] there was a significant family history of cancer in 28.6%. In the review of Stalker, Phillips, and Pemberton [10] the family incidence was 26.6%, whereas Barrett and associates,[7] found 26% of their cases also had a positive family background.

PREDISPOSITION AND MODE OF ORIGIN

The incidence of multiple primary malignant neoplastic disease based on the law of chance has been variously estimated in the neighborhood of 3%. The consensus seems to favor the theory that the actual incidence is greater than can be accounted for on the basis of chance alone.[11] The majority of reviewers of accumulated data believe that one cancer confers no immunity but that the reverse is true; that is, a second cancer is more likely to develop. Warren and Ehrenreich [8] have calculated that multiple malignant growths occur 11 times more frequently than the chance incidence. Lombard and Warren [12] recently observed that persons with skin cancers are predisposed to other skin cancers. Whether this susceptibility is caused by the first cancer or is inherent in the individual is not known.

White [13] explains the predisposition to multiple carcinomata in certain persons on the basis of the interaction of a functionally mature gene-bearing unit for cancer inheritance with one for localization, together with the necessary environmental stimuli.

In the light of these facts, it seems reasonable to consider that multiple malignancy is either an inevitable sequence in the course of uninterrupted neoplastic genesis or that susceptibility, resistance, and hereditary factors do exist. It also seems evident that the apparent and actual incidence of multiple primary malignant tumors should gradually rise because of the following reasons.

1. Progressive improvements in methods for accumulating accurate cancer statistics from all sources should bring more cases to light.

2. Progressive education of the laity, as well as the medical profession, should increase vigilance for the disease and result in earlier diagnosis and treatment.

3. Progressive increase in the number of persons living in the "cancer age" group should result in an increase in the incidence of multiple primary cancer as well as of initial cases.

4. Newer methods of treatment of existing cancers should lengthen survival times and increase cure rates, thus affording greater opportunity for multiple growths to occur.

Barrett and associates,[7] in discussing the various theories concerned in the genesis of multiple malignant neoplasms, state that the older theory of unicentric origin from a single cytologic focus has gradually given way to the theory of multicentric origin, wherein neoplastic transition may occur independently at two or more isolated points, either simultaneously or at variable intervals. Microscopic evidence of the multicentric origin of malignant neoplastic disease is commonly seen in lesions such as the intraepithelial epidermoid "carcinoma in situ" (Bowen's disease) and in the malignant degeneration of widely separated polyps of the colon. Ewing [14] has stated that "precancerous" or preinvasive anaplastic cytological changes can be demonstrated in areas outside the limits of the frankly invading carcinoma.

SITES OF MULTIPLE CARCINOMA

Table 2 from Slaughter [15] summarizes the frequency of the various sites of multiple malignancies. The 54.4% incidence in the same or paired organs substantiates Hurt and Broders'[9] opinion that multiplicity tends to occur in tissues of the same system. The skin was the organ by far most frequently involved. Rappin [16] reported a case of a 50-year-old woman with over 200 basal-cell carcinomata of the skin and Phillips [17] an instance of 23 microscopically verified skin cancers in one patient. The colon ranks second in order of organs involved by multiple malignancies. Dockerty [18] found polypoid carcinoma of the colon to be multiple in almost 40% of his cases. The skin and the colon are thus definitely sites which must be carefully searched for multple lesions.

Involvement of more than two types of tissue is rather rare. Warren's [5] report of 1078 postmortem examinations of patients with malignant tumors, including an extensive review of the literature, listed only three cases of triple primary carcinomata that originated in three different organs. As mentioned previously, the five cases listed in Table 1 all had three or more organs involved.

TABLE 1.—*Record of Five Patients with Four Successive Primary Malignancies*

Reference	1st Malignancy	2d Malignancy	3d Malignancy	4th Malignancy
Case 1 Holland, 1945 Woman, white	Aug., 1933; age 60; adenocarcinoma, right breast; subradical resection	June, 1939; squamous-cell carcinoma, Gr. 3, of thoracic esophagus; radiation therapy	June, 1939; basal-cell carcinoma of left cheek; radiation therapy	July, 1942; adenocarcinoma of colon; resection
Case 2 Goldman, 1945 Woman, white	1922; age 60; medullary carcinoma, left breast; radical mastectomy & radiation therapy	Oct., 1939; squamous-cell carcinoma in radiation scar, left chest area; wide excision through pleura	April, 1940; epidermoid carcinoma, Gr. 3, cervix; radium insertion & external radiation	May, 1941; adenocarcinoma, rectum; no treatment; died Nov., 1941
Case 3 Black & Hower, 1946 Woman, white	July, 1939; age 43; adenocarcinoma, right breast, Gr. 2, 1 cm. in diameter; radical mastectomy; no axillary involvement	June, 1941; adenocarcinoma, left breast, Gr. 4, 1 cm. in diameter; radical mastectomy; no axillary involvement	May, 1943; adenocarcinoma of uterus, Gr. 1; hysterectomy	Oct., 1945; adenocarcinoma, ascending colon, Gr. 2; wide resection & ileocolostomy
Case 4 Duncan, 1950 Woman, white	March, 1931; age 56; early epidermoid carcinoma, left labium majus; complete vulvectomy followed by radiation therapy	March, 1939; papillary adenocarcinoma of rectum near anus; locally excised plus insertion radium needles for 120 mg.-hr.	Aug., 1946; adenocarcinoma of uterine fundus; radium insertion for 4800 mg.-hr. plus radiation therapy to 4 pelvic parts for 22 treatments	March, 1949; basal-cell carcinoma of buttock; local excision
Case 5 Maddock et al., 1955 Woman, white	Nov., 1927; age 38; undifferentiated carcinoma of comedo type, right breast; radical mastectomy; no axillary involvement	March, 1940; age 51; papillary cystadenoma of right ovary with malignant degeneration; hysterectomy with biliary salpingectomy & oophorectomy	July, 1947; age 58; adenocarcinoma sigmoid colon, Gr. 2; resection; no lymph node involvement	May, 1948; adenocarcinoma, left breast, Gr. 3, duct-cell type; no metastasis to axillary lymph nodes found

Paired organs are often afflicted with cancer, the order of incidence in Slaughter's [15] report being breast, testes, ovaries, kidneys, and salpinges. Barrett and co-workers [7] found only the slight variation of breast, ovaries, testes, and kidneys. The high incidence of multiple malignancies in organs related by a basic sensitivity to, or production of, estrogenic substances is immediately apparent.

According to Slaughter's Table 2, the order of frequency of involvement of the gastrointestinal tract is, first, colon, second, combinations of colon and stomach, and, third, multiple lesions of the stomach. Multiple sarcomas are relatively rare. However, combinations of carcinoma and sarcoma are not infrequent.

TABLE 2.—*The Distribution of Multiple Tumors—Major Groups (Slaughter)*

	No. Cases	Per Cent
Carcinomas		
Multiple, of the same organ	749	40.0
Multiple, of paired organs	269	14.4
Total	1,018	54.4
G. I. tract, multiple, from mouth to anus	145	7.7
G. U. tract, multiple	18	0.9
Female genitalia, multiple	32	1.7
Skin, associated with G. I. tract	51	2.7
Skin, associated with G. U. tract	55	2.9
Skin, associated with breast	39	2.1
Breast and G. U. tract	65	3.4
Breast and G. I. tract	35	1.9
G. U. and G. I. tracts	120	6.4
Lung with other cancers	34	1.8
Miscellaneous, multiple	104	5.6
Sarcomas		
Multiple, in same organ	7	0.3
Multiple, of paired organs	16	0.6
Multiple, in different systems	3	0.1
Associated with carcinoma in same organ	35	1.8
Miscellaneous	91	5.0
Total	1,868	

BREAST CANCER

The distressingly high incidence of breast cancer and some recent interest in bilateral nonsimultaneous involvement of the breast makes it worth while to accord the breast a separate heading. Harrington,[19] from his tremendous experience with breast lesions, found 212 cases of nonsimultaneous carcinoma in the opposite breast, which, compared with his series of 6149 unilateral

carcinomas, gave the occurrence of a second breast lesion a percentage of 3.4. This, however, was the incidence of operable carcinomas found in the remaining breast in this series and not the total incidence of carcinoma occurring in the second breast. There was probably an equal number of cases, if not a greater number, in which primary carcinoma of the remaining breast developed but which was inoperable because of distant metastasis from the first side. Harrington felt that it was impossible to determine accurately the number of this latter group but believed that the actual incidence was probably from 6% to 8%. While this figure was relatively high, he did not think that it warrented mastectomy of the remaining breast. Haagensen's [20] follow-up showed involvement of the second breast in approximately 10%, half of the group being new primary and half being metastatic. He did not believe that this incidence called for routine removal of the second breast as a prophylactic procedure.

Keyes, Jordan, and Wyatt [21] believe that carcinoma will be found in the remaining breast after radical mastectomy in 12% of women in a carefully followed group and think that, if this occurrence continues its apparent rise, then one should consider removing the second breast shortly after the initial radical mastectomy.

Our own impression is that the finding of a lesion in the second breast is increased by periodic thorough follow-up examinations and will approximate 10%. In the case reported in this article, 21 years elapsed between the two breast cancers, and there is no doubt that both were primaries. In Slaughter's statistics the breasts accounted for more than 50% of the total multiple malignancies in paired organs. This figure may well be too low because a tumor in the second breast may often be erroneously considered metastatic from the first. If each lesion appears as a primary tumor and there is no evidence of intervening malignancy crossing from one breast to the other, as carcinoma erythematosum or "en cuirasse," then both lesions may well be primaries. Almost always a secondary involvement of the other breast shows signs of the crossing of the midline and usually of metastatic carcinoma elsewhere, e. g., the supraclavicular regions, lungs, bone, liver, etc.

Simultaneous bilateral breast carcinoma carries a very grave prognosis. Of Harrington's [19] group of 62 such patients, 44, or 71%, had nodal metastatsis at the time of the radical mastectomy. None of them survived to the 15-year period and only 3.3% lived 10 years. There were 18 cases, or 29%, with no axillary metastasis, and of these 5, or 40%, survived 15 years. From the surgeon's point of view, the important thing to be gained from these figures is to look for involvement of the other breast and to decide whether the second lesion is a metastasis or local extension from the tumor in the first breast or is an entirely new carcinoma. For the former cure is impossible, but palliation should be sought by every means. If it is the latter, cure is entirely possible and a radical mastectomy is indicated.

SUMMARY AND CONCLUSION

A case of four successive primary malignancies involving tissues of three different types is presented. All the tumors were treated surgically; three of them were cured, and the patient survived the fourth by seven years.

Four other cases of four primary successive malignancies were collected from the literature. Along with our case, all were women, all had a cancer of the colon or rectum, four of the five had a cancer of the female reproductive organs, four of the five also had a breast cancer, and two of the five had bilateral primary breast lesions.

A consideration of the frequency of multiple malignancies should alert every physician confronted with one tumor to look for a second cancer, both at the time of the original examination and at subsequent check-ups. For the follow-up, examination of the site of the original tumor and its common routes of extension is not enough. This should be done as frequently as indicated, and, in addition, every six months the cancer

patient should have an interval history with particular questioning on the common symptoms of cancer and a complete physical examination and laboratory study, especially covering the common sites of cancer occurrence.

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Treatment of Bleeding Esophageal Varices by Resection of the Lower Esophagus

Reestablishment of Esophagogastric Continuity by Means of a Polyethylene Tube

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INTRODUCTION

Although many operations have been devised for the treatment of bleeding esophageal varices secondary to cirrhosis of the liver, at present only three procedures are in fairly common usage. These are (1) the shunting of portal blood to the caval system, (2) the transesophageal ligation of the varices, and (3) the resection of the cardioesophageal region with esophagogastrostomy.

The advocates of the shunt operations emphasize the importance of lowering the portal hypertension, which is believed to be responsible for the development of the varices.* This may be accomplished by a satisfactory anastomosis between the portal or splenic veins and the inferior vena cava or left renal vein. Evidence of the reduction of portal pressure has been obtained at the operating table by measuring the portal pressure before and after the shunt has been performed † and also in the postoperative period by measuring the pressure in the varix through an esophagoscope.[10] On a theoretical basis the rationale of connecting the high-pressure portal system with the low-pressure caval system appears sound. However, in practice several unanticipated events seriously limit the value of this operation. When this technically difficult procedure is performed by experienced surgeons on patients with cirrhosis, a 20% mortality rate is obtained.‡ Indeed, an excellent paper by Linton [11] illustrates that the risk of surgery is even greater in those patients with ascites not responding to medical therapy, with a serum albumin below 3 gm. per 100 cc., with a prothrombin time more than four seconds above normal, and with a cephalin flocculation of 3+ to 4+. If one begins excluding these unfavorable candidates from this type of operation, the mortality will certainly be lowered, but a large proportion of the cirrhotic population with bleeding varices will be denied the possible value of surgical palliation of their disease. From the available literature it is almost impossible to estimate what per cent of the entire group are now being treated by this method. In a personal communication to Garlock in 1950,[7] Blakemore stated that he was able to perform a portacaval shunt on only one quarter of the patients he saw. If the experiences of others are comparable, then 75% of cirrhotic patients bleeding from varices cannot be helped by this type of surgery. This is a distinct drawback of the operation.

Once a shunt has been created, does it remain patent and does it protect the patient against recurrent hemorrhage? Postoperative bleeding might be considered an indication of the inefficiency of the shunt. In 50 survival cases operated upon by Linton

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* References 4, 5, 11, 21, and 22.

† References 4 and 5.

‡ References 4, 5, and 11.

between 1945 and 1951,[11] there were 9 patients who bled postoperatively, implying failure in 18%. These figures were very similar to those reported by Blakemore,[4] who had 32 postshunt bleeders in 136 cases (23%). Aside from the limitations of a 20% mortality, the need for selecting only the better-risk patients, and the occurrence of postoperative hemorrhages, there are also reports in the literature by other surgeons,§ who have not obtained the same percentage of good results as Blakemore, Linton, Welch, Child, and Jahnke.

The second procedure which is currently employed in the surgical treatment of patients with bleeding esophageal varices is the transesophageal ligation of the varices. Crile [6] has stressed the fact that bleeding hemorrhoids, which are probably related to increased pressures in the hemorrhoidal veins, are usually relieved by an adequate hemorrhoidectomy rather than by any attempts to reduce the venous pressures. Likewise, the bleeding "hemorrhoids" at the lower end of the esophagus should be surgically obliterated by several continuous ligations. Support for this concept is offered by seven reported cases [6] in which only two patients bled postoperatively during a 6- to 23-month follow-up, and in one of these a gastric ulcer was demonstrated. To be sure, this small series must now be much larger. If the results have continued as good as the initial report indicated, then this procedure, which is technically much less difficult than any venous shunt, should become more widely adopted. One might speculate that the remaining submucosal veins of the esophagus would be called upon to take over the load carried by three or four which have been ligated. After a period of time, the patient with portal hypertension might again have his varices. With this in mind, Linton [12] has utilized transesophageal ligation as a preliminary step in the control of patients in the acute stage of bleeding, rather than as a definitive operation. Since he observed recurrent hemorrhages during a short-follow-up period, he believes that a shunting procedure must be done after the initial severe hemorrhage has been controlled by the transesophageal ligation. Although it is still too early to evaluate fully the concept of merely ligating the varices, its technical simplicity and relatively low mortality make it a very attractive procedure and one which should be further explored.

The third surgical approach to the treatment of bleeding varices was introduced by Phemister and Humphreys [16] and consists of eradicating the source of the hemorrhage by resection of the distal esophagus and proximal stomach with esophagogastrostomy. The theoretical objection to this operation lies in the fact that, like transesophageal ligation, it does not correct the portal hypertension. If this factor is truly important, varices should re-form elsewhere, as in the remaining stomach pouch or esophagus. Bleeding might then recur. However, many observers are not entirely convinced that the lowering of the portal pressure is necessary for the control of the bleeding varix.‖ Several reports ¶ of small groups of cases with short follow-up periods suggest that the removal of the bleeding site may prove beneficial, but here also any final evaluation would be premature. At present, the main objection to this operation is that the mortality is high even in experienced hands.[16]

Removal of the lower end of the esophagus would appear to be the most logical approach, if it could be accomplished easily, quickly, and with a low mortality. The possibility of doing this was suggested by Berman's [1] procedure for the replacement of portions of the esophagus with a plastic tube for esophageal carcinoma. He observed that a new fibrous sheath formed around the plastic tube, and this fibrous sheath developed an inner layer of squamous epithelium within a year. Microscopic sections of the newly formed esophagus indicated that it should be quite adequate for conveying food into the stomach. This functional competency was proved by re-

§ References 8, 15, and 18; Blalock, A., in discussion on Linton.[11]

‖ References 8, 15, and 18; Berne, C. J., in discussion on Pattison [3]; Holden, D. W., in discussion on Berman and Hull.[9]

¶ References 19 and 20.

moval of the plastic tube in both animal and human experiments. Berman's last report [2] on using the plastic tube in 60 patients with carcinoma of the esophagus recorded a mortality of 10%. While the problem of leakage and esophagopleural fistulae had not been entirely solved, these did not seriously increase the morbidity of those patients whose esophagogastric continuity had been reestablished by the plastic tube. Modifications of the original technique for joining the tube with the esophagus are being experimentally studied by Berman,# and it seems likely that this technical complication of fistula formation will be overcome. However, even at this stage of development, the reported 10% mortality figure compares favorably with the mortality rate of those operations employed today for the treatment of esophageal varices.

Thus, the opportunity presented itself for the removal of that area, which is usually responsible for the patient's death, by an operation which is relatively easily accomplished.

REPORT OF CASES

The results with five cirrhotic patients who had bled from their esophageal varices were not as favorable as was anticipated. Obviously, the most favorable candidates were not available for this procedure, which was both new and experimental. Nevertheless, encouraging findings were noted during these experiences. The most objective evaluation is probably best obtained by a detailed report of the five patients upon whom this operation has been performed.

CASE 1.—A 50-year-old man was admitted to the Boston City Hospital on June 1, 1953, because of the vomiting of blood.

Present Illness.—For the past 20 years or more, the patient had ingested 12 to 15 "shots of rye" daily. About 18 months ago, he first noticed that he was jaudiced and was told by his family physician that he had liver disease. Six months before admission, he passed several tarry stools and vomited some blood. He was treated at home by his doctor and apparently was not seriously incapacitated. He had been well until one week ago, when he again passed some tarry stools, and the day previous to admission vomited large amounts of dark-red blood on four occasions. He became weak but did not faint. There had been no epigastric distress or abdominal pain of any type. There had been no recent swelling of his abdomen, jaundice, or ankle edema.

Past History.—The patient had been in good health most of his life. No serious illnesses, operations, or accidents were revealed in his history.

Physical Examination.—Temperature 99.8 F, pulse rate 108, respirations 26, blood pressure 130/78. The patient was a well-developed, well-nourished man who appeared older than his stated age. The positive findings included many spider angiomata over his face and chest, minimal jaundice of his sclera, a small amount of abdominal fluid, the liver enlarged to 4 fingerbreadths below his costal margin, and several large external hemorrhoids.

Laboratory Data.—The urine was normal, except for the presence of 4+ bile; hematocrit value 30; white blood cells 8200, with a normal differential count. Platelets were present; icteric index, 24; cephalin flocculation 4+ in 24 hours. Sulfobromophthalein sodium (Bromsulfalein) retention test was 24% at the end of 45 minutes. Total serum proteins were 5.8 gm. per 100 cc., with an albumin of 2.3 gm/100. Roentgen studies of the upper gastrointestinal tract revealed an irritable distal esophagus without varices and a duodenitis characterized by an irregular mucosal pattern. Esophageal varices were seen on esophagoscopic examination.

Hospital Course.—The esophageal bleeding was controlled by balloon tamponade. The patient required four transfusions to raise his hematocrit level to 36 and to lower his pulse rate to normal. During his preoperative preparation, he was occasionally uncooperative and confused. Another 1000 cc. of blood was given two days before operation, and on June 22, 1953, he underwent a resection of his esophageal varices, the lower 8 cm. of his esophagus being replaced by a 10-cm. polyethylene tube. He withstood the operative procedure quite well, having been carried at a light level of anesthesia throughout. On the second postoperative day he pulled out the Levin tube which had been placed through the esophagus and polyethylene tube into his stomach. On the sixth postoperative day he was mistakenly given a full breakfast by a relief nurse, and his egg and coffee were noted to have drained out of the left chest through his intercostal drainage tube. He had very little febrile or systemic reaction to his esophagopleural fistula even though a culture yielded staphylococci, Hemophilus influenzae, Aerobacter aerogenes, Pseudomonas aeruginosa (Bacillus pyocyaneus), and fusiform bacilli. Attempts to control the drainage by chest suction and suction on a Levin tube placed down his esophagus to the fistulous site were partially successful, until he again began pulling out his tubes. Because the fistula was not closing and the patient seemed to be gradually

Berman, E. F., personal communication.

deteriorating, a gastrostomy was performed under local anesthesia on the 10th postoperative day. Gastrostomy feedings were begun, while the fistulous opening was kept on suction through a constantly replaced Levin tube. On the 17th postoperative day some of his gastrostomy feeding was mistakenly given through his esophageal Levin tube, after which he became somewhat dyspneic, suggesting tracheal aspiration. His urinary output decreased, he lapsed in a comatose state, and he died on the 18th postoperative day.

Pathological Report.—Surgical specimen revealed esophageal varices. At postmortem examination the distal esophagus was replaced by a 4-in. polyethylene tube. There seemed to be some occlusion at the proximal anastomosis by redundant esophageal mucosa. In one area there was a fistulous opening measuring about 3 mm. in diameter which communicated with the mediastinum and left thoracic cavity. There was no significant mediastinitis or empyema. The lungs were air containing. In the abdomen, there was a moderate amount of ascitic fluid and a small, severely fibrotic liver.

Comment.—This 50-year-old man had his liver disease recognized 18 months before he was admitted with hematemesis and melena. The hemorrhage was determined by esophagoscopy to originate from varices, and he was treated by balloon tamponade and 2000 cc. of blood. On June 22, 1953, the lower esophagus was removed and a polyethylene tube was inserted. The postoperative course was complicated by his unexplained removal of the Levin tube, by mistakenly being given a full breakfast on the sixth postoperative day, by the development of a esophagopleural fistula, and by the aspiration of some of his gastrostomy feedings which were mistakenly put into his esophagus. He died in hepatic coma on the 18th day following operation. The important information gained was that this surgical procedure was well tolerated under a light plane of anesthesia by a patient with a badly diseased liver, whose hepatic functions showed a sulfobromophthalein sodium retention of 24%, an albumin of 2.3 gm. per 100 cc., and a cephalin flocculation of 4+.

CASE 2.—A 39-year-old married housewife was first admitted to the Boston City Hospital in August, 1953, complaining of nausea and of having vomited blood.

Present Illness.—According to her husband, the patient had always been a drinking woman but still seemed to consume an adequate diet. Preceding her admission, she had had six or seven cocktails and on the day of admission at least three. She had apparently been in good health, until the evening of admission, at which time she developed nausea, and this was followed in a few minutes by the vomiting of bright-red blood. There had never been any significant abdominal pain, jaundice, abnormal stools, or previous episodes of hematemesis in her previous history.

Physical Examination.—The patient did not appear to be in any distress. Her temperature was 98.6 F, pulse rate 108, respirations 20, and blood pressure 98/60. There was a generalized icterus, multiple spider angiomata over the arms, a liver edge felt 2 cm. below the costal margin, and a spleen almost reaching the iliac crest. There was some question as to the presence of ascites. In addition, a right femoral hernia was noted.

Laboratory Findings.—Revealed a hemoglobin level of 6.5 gm., sulfobromophthalein retention of 78%, cephalin flocculation 3+, prothrombin time 15 seconds with a control of 13, and an albumin of 1.7 gm. per 100 cc.

Hospital Course.—While being transported to the wards, the patient vomited a measured 2100 cc. of blood and gastric juice. She was given a transfusion, and esophageal ballon tamponade was accomplished. After 36 hours, bleeding appeared to have stopped and the tube was removed. On the fifth hospital night she began to bleed again, her pressure fell to shock levels, and she became restless and then unresponsive. With transfusions the blood pressure returned to normal, but her coma deepened. Because of her desperate state and the recent reported value of corticotropin (ACTH) and cortisone in hepatic coma, the medical consultants decided to try this therapy, which was begun on the seventh hospital day. Over the next five days, either because of or in spite of the hormone therapy, the patient gradually came out of her hepatic coma. During her convalescent period, x-ray studies revealed esophageal varices and prepyloric scarring on the lesser curvature of the duodenum. Splenic aspiration and bone marrow biopsy revealed no evidence of any blood dyscrasia. Since she was considered too poor a risk for a shunt procedure, she was discharged to the follow-up clinic on the 64th hospital day.

Second Admission.—Although her liver status seemed to improve over the next three months, she was awakened at 3 a. m. on Jan. 12, 1954, because of severe nausea, and she began vomiting bright-red blood. She was brought to the hospital by 6 a. m., transfusions were started, and a Sengstaken-Blakemore tube was inserted. The tamponade was not effective, and she continued to regurgitate blood. Because she was bleeding to death from her ruptured varices, multiple transfusions were rapidly given,

and she was taken to the operating room, where the varices were removed and the esophageal continuity reestablished with a 10-cm. polyethylene tube. She seemed to take the operative procedure fairly well, in that her blood pressure remained normal and her urinary output was good, but 14 hours postoperatively she became restless, then somnolent, and, finally, comatose. She remained in coma almost 48 hours and this time died without any benefit from the corticotropin and cortisone.

Pathological Findings.—The surgical specimen revealed esophageal varices. At postmortem examination the plastic tube was in place in the mediastinum. There was a small amount of cloudy yellow fluid in the left thorax. The liver was slightly enlarged and grossly scarred. The spleen was markedly enlarged, but there was no significant ascitic fluid.

Comment.—This young woman had passed into a hepatic coma five months before her first admission, after a moderate hemorrhage. She recovered and seemed to show gradual improvement in her hepatic functions when the second and more massive hemorrhage occurred. Regardless of how the bleeding was to be controlled, another episode of hepatic coma was anticipated. Realizing that nonsurgical methods were not influencing the exsanguinating hemorrhage, and fortified with the knowledge that some patients survive a second episode of hepatic coma, it was decided to operate upon her. Unfortunately, the successful surgical control of her hemorrhage was not followed by a successful recovery from the expected hepatic coma. This began about 14 hours postoperatively and lasted until her death, 48 hours later.

CASE 3.—This was the 18th Boston City Hospital admission of a 46-year-old meat cutter who was vomiting blood.

Summary of Previous Admissions.—

First Admission: Nov. 24, 1949, to Nov. 26, 1949.

Diagnoses: (1) Acute and chronic alcoholism, (2) alcoholic gastritis.

Second Admission: Aug. 18, 1952, to Sept. 25, 1952.

Diagnosis. Laennec's cirrhosis, decompensated.

Third Admission: Oct. 5, 1952, to Nov. 29, 1952.

Diagnoses. (1) Laennec's cirrhosis, decompensated, (2) portal hypertension and ascites, and (3) chronic alcoholism.

Fourth to Fifteenth Admission: One-day admissions during the first eight months of 1953 for paracenteses.

Sixteenth Admission: Dec. 10, 1953, to Jan. 17, 1954.

Diagnoses. (1) Laennec's cirrhosis, (2) bleeding peptic ulcer.

Seventeenth Admission: May 5, 1954, to May 15, 1954.

Diagnoses. (1) Laennec's cirrhosis, (2) esophageal varices with a minor hemorrhage.

Present Illness.—Thirteen days after his discharge, the patient began to vomit bright-red blood. There was no abdominal pain this time as was present on his 16th admission, when an ulcer was found. There was no recent ingestion of alcohol.

Physical Examination.—Temperature 100.4 F, pulse 106, respirations 20, blood pressure 112/70. The patient was an apprehensive emaciated man who looked older than his stated age and appeared to be in impending shock. The liver was slightly enlarged, but the spleen could not be felt. There were no ascites or jaundice. The epigastrium was nontender.

Laboratory Data.—The hematocrit level was 32, white-blood-cell count 9900, and urine, normal. Sulfobromophthalein retention was 27%, cephalin flocculation 1+, albumin, 2.1 gm. per 100 cc. icterus index 25, and prothrombin time 16.6 seconds with a control of 13.2 seconds. An x-ray taken one month previously had suggested the possibility of esophageal varices.

Hospital Course.—A triple-lumen single-balloon tube was inserted and the bleeding source identified as the esophagus. Tamponade was successfully accomplished. During the first 13 hours, the patient received four pints of blood, and the hematocrit level rose to 35. The lower esophagus was resected through the left chest and a 10-cm. polyethylene tube used to reestablish continuity between the esophagus and the stomach. The postoperative course was only complicated by a superficial thrombophlebitis at the site of a cut-down. He was discharged on the 23d postoperative day taking a soft-solid diet.

Follow-Up.—About three months after his varices were removed, the patient began to get a gnawing sensation in the pit of his stomach similar to the pain he had when his x-ray demonstrated an ulcer. This occurred about the same time that he began having disagreements with his employer. The arguments continued; the pain became worse and not entirely relieved by the antacids which he took himself. At four months and at eleven months after his operation he passed a few tarry stools. There was no vomiting or weakness associated with these stools but only the constant epigastric pain. He was hospitalized on both these occasions, but a definite ulcer could not be found on careful x-ray study. However, with antacid therapy the pains subsided and the stools rapidly became guaiac nega-

tive. Because he had sustained two minor episodes of bleeding postoperatively and because his liver functions were better than at the time of his operation, the decision to perform a portacaval shunt was made by another surgeon, under whose care the patient had come. Thirteen months after his esophageal varices had been removed, the shunting procedure was performed with hypothermia and with cyclopropane anesthesia. His postoperative course was stormy, and, after four weeks, he died in hepatic failure. An autopsy was not obtained.

Comment.—This was a complicated problem in a cirrhotic patient who had both ulcer and varices. The use of a single-balloon triple-lumen tube * helped both to identify the varices as the bleeding source and to tamponade the hemorrhage. With a sulfobromophthalein retention of 27% at the end of 45 minutes, chemically tested jaundice, and a serum albumin of 2.1 gm. per 100 cc., the patient satisfactorily withstood the removal of his esophageal varices. The appearance of two minor bleeding episodes, as manifested by tarry stools, was discouraging. Equally disturbing was the inability to demonstrate a peptic ulcer roentgenologically, despite the fact that the tarry stools were associated with gnawing epigastric pain, which appeared during a period of nervous tension and which was satisfactorily treated by antacids. Although he survived for 13 months after the resection of his esophageal varices and although his liver functions showed improvement at that time, he was not able to withstand a portacaval shunting procedure and died one month after the second operation.

CASE 4.—A 38-year-old married clerk was first admitted on May 14, 1954, after he had vomited material which looked like "pieces of liver."

Present Illness.—Seven months previously, the patient had entered another hospital for the repair of an umbilical hernia. At that time, the diagnosis of cirrhosis was first made. He was readmitted at the same hospital two months ago, after a spontaneous rupture of the previously repaired hernia. On the sixth postoperative day, he began to vomit large amounts of bright-red blood, which were controlled with multiple transfusions and balloon tamponage. He went through a period of disorientation for several days and was thought to be in a hepatic coma. When the coma disappeared and the bleeding ceased, the diagnosis of esophageal varices was confirmed by x-ray studies, but the patient was considered too poor a risk for a portacaval shunting procedure. From the time of his original umbilical herniorrhapy until his admission to the Boston City Hospital (a seven-month period), 10 paracenteses were performed.

On the night prior to admission, he suddenly vomited blood clots, without any associated abdominal pain. There was no history of jaundice.

Past History.—The patient had enjoyed good health most of his life. For 20 years he had been consuming large amounts of alcohol (1 pt. of whisky and 15-20 glasses of ale daily). He did not believe that his food intake was decreased because of his drinking.

Physical Examination.—Temperature 98.6 F, pulse rate 96, respirations 16, blood pressure 120/60. There were numerous spider angiomata over his back, neck, chest, and arms. The abdomen was markedly distended and tense. Because of the fluid, his liver and spleen could not be felt. The umbilicus was absent and replaced by a scar. Many dilated veins coursed over the abdominal wall. The scars of the multiple paracenteses were apparent. There was 2+ leg edema.

Laboratory Data.—Hemoglobin 5 gm. per 100 cc., hematocrit 22, white blood cells 12,000, with a normal differential. Platelets were present. The urine contained no abnormalities. The sulfobromophthalein retention test was 33% at the end of 45 minutes. Cephalin flocculation was 3+; icterus index, 8. Total proteins were 6.3, with an albumin of 2.2. Prothrombin time was 14.6 seconds, with a control of 13.

Hospital Course.—He began to vomit bright-red blood on the day of his admission. For two and one-half days esophageal balloon tamponage was applied and multiple transfusions were given. With the bleeding under control he improved, but the ascites required frequent removal to alleviate his discomfort and respiratory distress. It was decided to follow him for a few months as an outpatient on a diet completely lacking in salt.

Interval Note.—During an 11-week period his ascitic fluid gradually decreased, his face and extremities became fuller, and his strength improved. His weight fell from 250 to 214 lb.

Readmission for Operation.—On examination, the temperature, pulse, and respirations were normal. There were multiple spider angiomata, but no icterus present. There was some fluid in the abdomen, but on this occasion his liver was readily

* This tube may be obtained from the Davol Rubber Company, Providence 2, R. I. The clinical studies demonstrating its value have been published in the report, "The Use of a Triple-Lumen Single-Balloon in the Diagnosis and Treatment of Massive Upper Gastrointestinal Hemorrhage," Surgery **38**: 667, 1955.

palpable 4 fingerbreadths below both costal margins. The spleen could not be definitely outlined. Slight edema of the extremities persisted.

The laboratory data on this admission showed slight improvement in the sulfobromophthalein retention, which fell from 33% to 15%, and an increase in serum albumin from 2.2 to 3.6 gm. per 100 cc. The cephalin flocculation remained 4+.

Hospital Course (Second Admission).—On Sept. 24, 1954, the lower portion of the esophagus, with its prominent submucosal varices, was removed, and a 3 in. polyethylene tube used to reestablish esophagogastric continuity. The postoperative course was remarkably uneventful, and the patient was discharged on the 21st hospital day.

Follow-Up.—During the two-month period after his varices had been removed, the patient had to be readmitted for several days because of dysphagia and back pain. No abnormalities were found. This quickly improved, as did his appetite and strength. He plans to return to work in the near future.

Comment.—This patient came to the hospital because of a second massive hemorrhage from his esophageal varices. He had recovered from his initial hemorrhage, which was associated with hepatic coma and which occurred seven months previously. During this period, he received many paracenteses. After being considered too poor a risk for a shunting procedure, he seemed to improve and then tolerated uneventfully an operative procedure for removal of the pathological site, which constantly presents a threat to the life of the patient who has once ruptured his esophageal varices. The early observation period in this patient has been encouraging.

CASE 5.—A 61-year-old widower was admitted to the Boston City Hospital for the fourth time, on Oct. 8, 1954, after having vomited a pint of blood.

Present Illness.—In March, 1952, the patient noted some swelling of his abdomen, which increased and was associated with both a loss of appetite and sense of ill health. He sought hospitalization for the first time in August, 1952, at which time the diagnosis of Laennec's cirrhosis was made. After a paracentesis, he showed no tendency toward reaccumulation of the fluid and was fairly well until May, 1953, when he became nauseous and vomited a cupful of blood. At that time there was also some soreness in his epigastrium. During this second hospitalization, x-ray studies revealed esophageal varices and a deformed duodenal cap suggesting a chronic duodenal ulcer. With transfusions and balloon tamponade the bleeding was controlled. At the time of discharge, the source of his hemorrhage could not be definitely attributed to either the varices or the ulcer. His third admission occurred two months later, when he was found confused and febrile. The exact explanation for these conditions was never determined, but they disappeared spontaneously during a 10-day period.

For the next twelve months, he remained in fairly good health. Three days prior to this admission he awakened in the morning and vomited some bright-red blood. He ignored this episode and continued to eat normally, even though he vomited again the next day. Finally, while walking to the bathroom, he fell to the floor from weakness and vomited a considerable amount of blood. On seeing this, his landlady sent him to the hospital. There had been no abdominal pain with his present illness.

Past History.—Aside from the three previous admissions to the Boston City Hospital during the past two years, the patient had enjoyed excellent health.

Physical Examination.—Temperature 98.4 F, pulse rate 120, respirations 18, blood pressure 90/30. The patient was a well-developed, poorly nourished elderly man with a ghostly pallor who was fairly well oriented, except as to time. The liver edge was felt two fingers below the right costal margin, but there was no fluid, splenomegaly, or abdominal tenderness.

Laboratory Data.—The urine was normal, except for 10-12 white blood cells per high-power field. Hemoglobin was 4 gm. per 100 cc. and hematocrit level 13. WBC 8700, with a normal differential. The sulfobromophthalein retention was 40% at the end of 45 minutes; cephalin flocculation, 2+; icterus index, 10; total protein, 5.0 gm. per 100 cc. prothrombin time was 16.4 seconds, with a control of 13.1.

Hospital Course.—He received 7000 cc. of blood over a six-day period, while the esophageal bleeding was identified and controlled by means of the triple-lumen single-balloon tube. X-ray studies confirmed the diagnosis of varices, showed a moderate hypertrophic gastritis, and were negative for peptic ulcer. On the 10th hospital day, the esophageal varices were resected. To say that this patient had a stormy postoperative course is to grossly understate the case. He developed a virulent empyema of his left thorax, which on culture showed hemolytic Micrococcus aureus var. albus (Staphylococcus aureus), A. aerogenes, enterococci, and alpha-hemolytic Streptococcus. He manifested signs of liver decompensation by the appearance of ascites, marked enlargement of his liver, jaundice, and a rise in his cephalin flocculation, to 4+. On the 12th postoperative day an esophagopleural-cutaneous fistula was noted. However, with vigorous and heroic therapeutic efforts on the part of the resident house staff, which consisted of intravenous antibiotic ther-

apy, thoracenteses, closed thoracotomy drainage, blood transfusions, and tube feedings, the patient survived the postoperative complications. The empyema healed slowly after drainage, and the esophagopleural-cutaneous fistula closed. The patient is still being treated for his ascites, which is responding poorly.

Comment. — This patient illustrated the problem that many of our cirrhotics present. On the second admission to the hospital he was found to have both varices and an ulcer deformity on x-ray examination; hence, the exact source of the hemorrhage could not be definitely proved. On his present admission, however, the use of the triple-lumen single-balloon tube identified the varices as the bleeding site. An encouraging observation was the fact that this patient, with a sulfobromophthalein retention of 40% and a serum protein of 5 gm. per 100 cc., withstood the operative procedure quite well. In addition, he survived the grave complications of a staphyloccal empyema and esophagopleural fistula.

GENERAL COMMENT

The cirrhotic patient who enters the hospital bleeding from a ruptured esophageal varix has a poor outlook. From several earlier control studies † it was learned that at the end of one year following the initial hemorrhage only 30% of the affected cirrhotic patients remained alive. A more recent review [14] indicated that better treatment of the diseased liver and the use of antibiotics have forestalled many untimely deaths from hepatic failure and infections. However, hemorrhage has continued to remain as ominous an occurrence as always, despite the use of liberal blood transfusions and balloon tamponade. Furthermore, 95% of those patients who have had a hemorrhage from their varices will die from a subsequent hemorrhage or its associated complication of hepatic coma.[14] Thus, it is apparent that the natural life expectancy of cirrhotic patients with bleeding varices is even less than that of patients with many of the common malignancies.

† References 17 and 13.

Not only is some surgical procedure necessary to eradicate the varix which has once ruptured, but the operation should be one which the patient with a badly diseased liver can withstand. In addition, since 60% of these patients die during their first bleeding episode, it is also necessary that the operative procedure be one which can be carried out under emergency circumstances. Finally, the surgical trauma should not produce further damage to the liver.

The operation which is being proposed in this paper is one which on theoretical grounds might fulfill these requirements. The reported experience with five patients suggests that the patient with a badly diseased liver can withstand the operative trauma of a three-hour thoracotomy, carried out in a fairly light plane of anesthesia. The first patient, who died in hepatic coma 18 days postoperatively, developed complications which probably had more to do with his liver failure than the operative procedure itself. Since there was no significant change in his general status or his liver functions during the early days following operation, it is reasonable to assume that, if the postoperative complications had not occurred, the fatal hepatic failure would have been averted. The second patient had lapsed into hepatic coma previously, after a milder hemorrhage than the one which necessitated surgical intervention. Although it seems likely that she would have succumbed to either hemorrhage or coma without operative treatment, the contributing role of the operation to her death cannot be entirely discounted. Fortunately, the other three patients with severely damaged livers survived their operation. It should be noted that two of these five patients were considered unacceptable for a portacaval shunt. Furthermore, in two there was persistent ascites, in four the sulfobromophthalein retention was greater than 20%, and in four the serum albumin was below 3 gm. per 100 cc. Linton's series [11] revealed that the mortality among the patients selected for a shunt procedure was 44% in those with ascites, 19% in those with the sulfobromophthalein retention above 10%, and 83% in

those with serum albumin below 3 gm. per 100 cc. From these mortality figures relating to liver functions, it is evident that even more disastrous results would have been encountered had our five patients been subjected to a shunt procedure.

Since it has been shown by Crile [6] and others [12] that transesophageal ligation can be carried out in the active phase of the hemorrhage, it is reasonable to assume that the procedure described here, of resecting the lower esophagus and reestablishing intestinal continuity with a plastic tube, should also carry a permissible mortality. The anesthesia, surgical trauma, and duration of the operation, which constitute the surgical risk, are almost identical in the two procedures. Whereas the patient who was operated upon during the active bleeding period did succumb (Case 2), there is little reason to expect this occurrence in every case. On the other hand, nonoperative management of a patient who cannot be controlled with multiple blood transfusions and balloon tamponade is uniformaly fatal.

There are two theoretical considerations which might be used in argument against the operation proposed here. If the complication of esophageal fistula formation resulting from poor healing between the plastic tube and the esophagus cannot be overcome by technical improvements in the method of anastomosis, then many cirrhotic patients will not be able to survive this added insult. Secondly, the obstruction to the drainage of the submucosal veins of the stomach by the removal of the lower esophagus might increase both the size of the gastric varices and their tendency to bleed. It is not necessary at this time to review the several explanations which have been proposed as to why the varix at the lower end of the esophagus is the most vulnerable site in the entire hypertensive portal system. The fact is well established that, when a ruptured varix is demonstrated at postmortem examination, it is nearly always located within a few centimeters of the cardioesophageal junction. Whether the submucosal gastric veins will represent the same threat to the life of the cirrhotic patient when the lower esophagus has been removed remains to be determined. It is hoped that the operative procedure suggested herein will be employed in other clinics so that a sufficiently large number of patients will be available for follow-up studies. In this way, the validity of the two theoretical objections to the operation will be substantiated or invalidated.

In evaluating operations for cirrhotic patients with bleeding esophageal varices, two categories should be considered. First, what are the surgical results in those patients operated upon during the active phase of the bleeding? Since about 60% of the patients with this disease die during the inital bleeding episode without surgical treatment,[14] any operation that might be undertaken in the active phase would certainly be associated with a high mortality. Nevertheless, if a significant number of patients could be salvaged, there would be little doubt as to the merit of the operation. However, in the second category, the elective group, the evaluation of the surgical procedure employed must be based on different facts. It has already been noted [14] that supportive medical management will protect two out of three patients during the first year after they have survived their initial hemorrhage. A worthy operation for the patients in this group would be one that carries a low mortality and one with which at one year postoperatively more than 66% of the patients are still living.

Two of the three operations in use today (the venous shunts and the resections with anastomoses) have not proved feasible for salvaging the 60% of the cirrhotic persons who die during their initial hemorrhage from varices. Transesophageal ligation of varices does include these patients, but some consider this operation only an emergency procedure, to be followed by a venous shunt at a more propitious time.[12] Whether any of the elective operations performed for esophageal varices alters the natural course of this disease remains to be determined.

SUMMARY

Resection of the lower esophagus and the reestablishment of intestinal continuity with

a plastic tube is suggested as a means of treating bleeding esophageal varices.

Of five patients subjected to the procedure, the first two died during the early postoperative period, and the other three were alive 13, 10, and 9 months, respectively, after their operation.

The experience gained from these cases suggests that cirrhotic patients with badly diseased livers can withstand the operative procedure if complications do not occur. Two of these five patients were considered unacceptable for venous shunts.

The attractiveness of the procedure lies in the technical ease with which it may be accomplished, the relatively short operating time required, and the light plane of anesthesia that is permissible. Furthermore, it removes the pathological area which precipitates or causes the death of most of these patients.

The utilization of the procedure might be restricted if the technical complication of fistula formation cannot be reduced and if gastric varices develop in place of the resected esophageal varices.

Before any conclusions can be drawn concerning the value of this operation many more patients will have to be treated and a one-year follow-up obtained. Because the number of these patients under the care of one physician is not very great, it is hoped that this operation will be employed and evaluated in other large clinics.

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An Apparatus and Technique for Freeze-Drying Arterial Homotransplants

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The concept of arterial storage and substitution, as developed experimentally by Carrel * and Guthrie [12] at the turn of the century and later successfully applied clinically by Blakemore,[3] Hufnagle,[13] and Gross,[11] is now established as a practical and dependable procedure. A growing clinical experience with arterial substitution, as reported by Dubost,[9] Swan,[25] Julian,[17] and De Bakey and Cooley,[8] has further emphasized the usefulness of arterial homotransplantation in the surgical management of obstructive and aneurysmal diseases of the major vessels. Until such time as the synthetic fiber fabric substitutes demonstrate an equally satisfactory solution to both large- and small-vessel substitution problems, it would appear worth while for the surgeon treating these conditions to have access to stored arterial homotransplants. Among the several methods of arterial transplant storage currently in use, the freeze-drying technique has been found most desirable by many investigators.† The most conspicuous advantage of this method is that of prolonged storage at ambient temperatures as compared with the four- to six-week period allowed with 4 C storage in serum and the six- to nine-month interval with dry ice preservation. Histologic preservation, maintenance of tensile strength, and the early results following host substitution of the transplant have been found to be essentially comparable whether viable (near or below freezing temperatures) or nonviable (freeze-drying) storage methods are utilized.[21] The results achieved with other methods of nonviable storage have appeared in the current surgical literature.‡

The original application of the principle of drying tissue from the frozen state was made in 1896 by a German zoologist Altman,[1] who developed the technique for processing fixed tissue sections. The process was applied to biologic materials initially by Shackell,[24] in 1909, followed by the processing of freeze-dried antisera for clinical use by Florsdorf,[10] in 1933.

The process as practiced at the present time consists of first extracting extracellular water from frozen tissue followed by the slower removal of bound, intracellular water. Extraction is accomplished through the sublimation of moisture from the frozen state. The vapor pressure of water is reduced within a closed system to a low level, i. e., $\times 10^{-3}$, by means of a refrigerated trap using dry ice or liquid nitrogen to condense and freeze the moisture vapor. A vacuum is maintained within the system to facilitate the molecular flow of water vapor. After adequate drying the processed tissue is sealed in a nearly oxygen-free atmosphere, either by the use of an inert gas, such as dry nitrogen, or within a vacuum. It is generally believed

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* References 4 to 7.

†References 2, 8, 14, 15, 16, 19, 21, and 23.

‡ References 18 and 20.

that residual moisture levels should not be above 2% to 5% and preferably below 1%.[21] It would appear at the present time that satisfactorily processed tissue may be stored under these conditions for at least a period of years, if not indefinitely. Proteins, particularly those of immunologic interest, undergo little alteration during freeze-drying other than an increase in solubility. There is evidence to indicate that some proteins become less antigenic in the case of arterial tissue.[21] Carbohydrates and especially fats are somewhat less well preserved by this process; therefore anaerobic metabolism must be minimized by storage in an atmosphere nearly void of oxygen. Tissue architecture is only slightly altered by progressive crystallization of ice during freezing and thawing of this type. The size and rate of crystal formation may be minimized by maintaining low temperatures.

APPARATUS

The freeze-drying equipment used in the tissue bank of the department of surgery, State University of Iowa College of Medicine, was designed and developed as a nonbreakable metal apparatus which would utilize dry-ice condensers for water extraction. The slightly greater efficiency of liquid nitrogen traps is outweighed by the expense and procurement problems. The equipment, which is constructed of ⅛ in. thick brass consists of a primary-manifold-type dry-ice condenser, 6 in. in diameter, connected to a 2-in. oil diffusion pump § (Figs. 1 and 2). The latter is backed by a 33-liter/min. two-stage Duo-Seal vacuum pump. A secondary dry ice condenser is placed in the vacuum line immediately distal to the oil diffusion pump. Stainless steel pipe 2 in. in diameter is used where the vacuum line enters or leaves a condenser so as to minimize heat loss by conductance. Vacuum connections throughout are obtained through the use of "O" ‖ ring seals, which permit ready disassembly and cleaning. The Pyrex glass tissue tubes,¶ which are sized at the open ends to 1 in. ±.010, are attached to the manifold condenser using these same seals (Fig. 2). A maximum of 10 tissue tubes may be processed at one time. A thermocouple vacuum gauge # has been found to be a reliable and sturdy gauge for registering the vacuum within the system. A jacket composed of 2 in. of Fiberglas insulation covered by canvas encloses the manifold condenser during operation of the equipment.

§ National Research Corporation, Cambridge, Mass.

‖ Linear Inc., Philadelphia.

¶ E. Machlett & Sons, New York.

National Research Corporation, Cambridge, Mass.

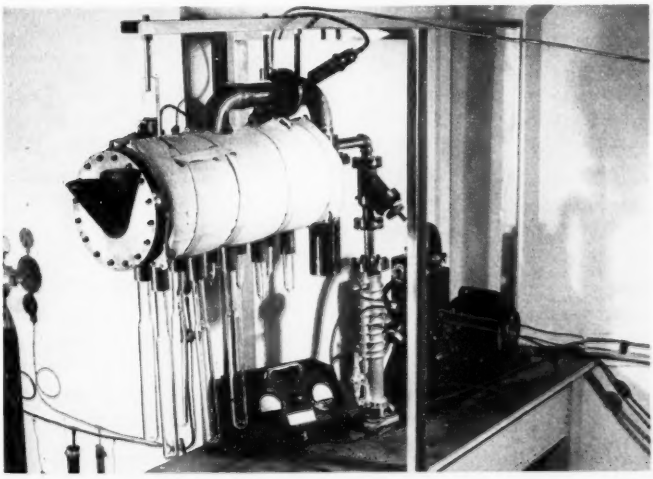

Fig. 1.—Showing the freeze-drying equipment assembled for processing tissue.

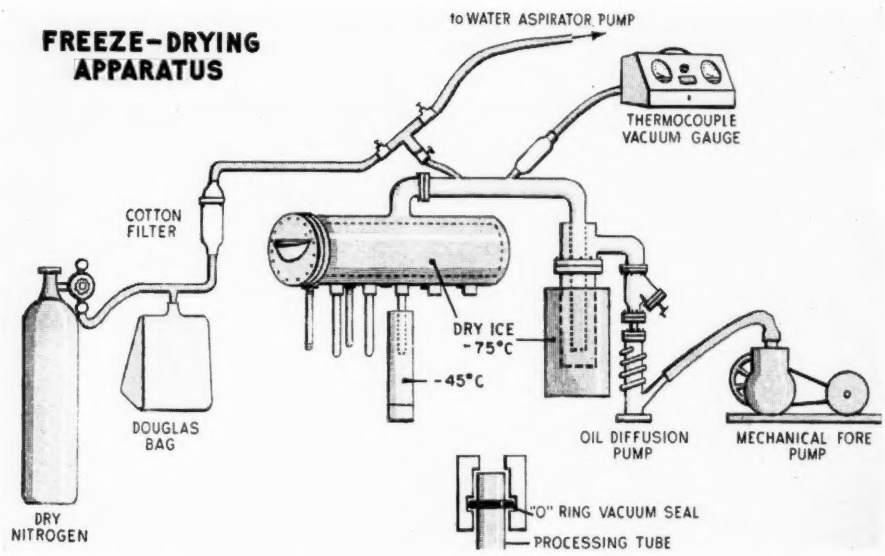

Fig. 2.—A diagrammatic illustration of the freeze-drying equipment. Dry nitrogen is used to break the vacuum. See text for explanation.

PROCEDURE

Donor tissue, taken without sterile precautions at the time of necropsy, is stored in a dry-ice chest until 8 or 10 vessel segments have been accumulated. The tissue is thoroughly washed in saline, trimmed of excess adventitial tissue, and frozen in a dry ice-alcohol bath prior to storage. Vessel branches are left 1 cm. long and untied. After attachment of the tissue tubes to the manifold, a 9:1 mixture of carbon tetrachloride and chloroform in dry ice is placed about the tubes during the first hour of processing. This mixture maintains the frozen tissue at approximately —45 to —50 C until the vacuum within the apparatus is sufficiently low, i. e., 50μ, to keep the tissue at —30 C by virtue of the loss of heat of sublimation. As drying proceeds, the tissue temperature gradually rises, eventually reaching room temperature when drying is nearly complete. The major portion of the moisture is rapidly extracted in the first four to six hours. A vacuum of 5μ to 10μ is maintained, this being regulated by a large-bore in-line valve. A pressure lower than 1μ is undesirable when using dry-ice traps, inasmuch as the vapor pressure of water at this temperature is approximately 1μ and a vacuum higher than this will sublimate the moisture frozen on the traps, allowing it to enter and foul the vacuum pumps. After completion of the first eight hours of processing, the vacuum is broken by introducing dry nitrogen into the system through a valve-controlled side-arm. The tissue tubes are removed and the vessel segments sterilized by covering them with ethylene oxide for 30 minutes after the method of Hufnagel.[14] The ethylene oxide is decanted at the end of this period and the tissue tubes replaced on the manifold condenser. The dry ice chamber is removed from the manifold condenser and replaced by an end-plate. Residual adsorbed ethylene oxide is removed through a side-arm connected to a water aspirator pump. The latter step is necessary prior to reestablishing the vacuum, since the residual ethylene oxide with a freezing point of —111 C will not be prevented by the trap from passing into and fouling the forepump oil. A qualitative trace test has been developed to determine the necessary period of time required to remove residual ethylene oxide. This step usually

requires 30 minutes for completion. The secondary condenser is then allowed to carry the system overnight. The following morning, or some 24 to 30 hours after beginning the processing period, a short segment of each tissue tube is narrowed to capillary size under atmospheric pressure using a gas-oxygen torch. Dry nitrogen admitted to the system through a side-arm is used to break the vacuum. A secondary vacuum of 10 μ is rapidly developed and the final sealing-off carried out at this pressure with a fine-tipped

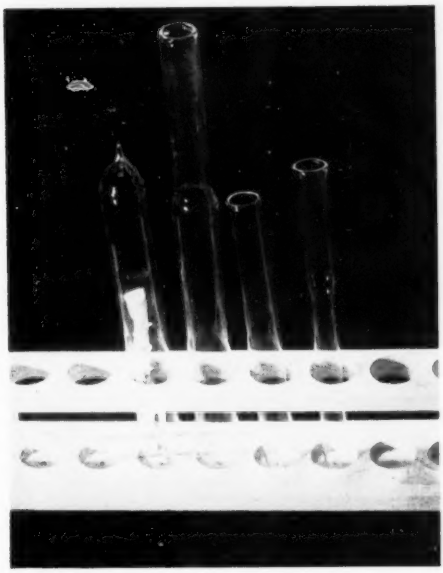

Fig. 3.—The three sizes of tissue tubes used for processing human and experimental homotransplants. The type of glass seal obtained by the technique described is also shown.

gas-oxygen torch. The glass seals obtained by this technique have been found to be lasting and reliable.

COMMENT

Rapid and dependable freeze-drying requires an apparatus with the following characteristics:

1. Dependable vacuum connections
2. Close proximity of tissue and condenser surface
3. Large condenser surface area
4. Large-bore, short vacuum lines without constrictions or excessive bends
5. Vacuum pumps of adequate volume
6. Reliable and sturdy vacuum gauging
7. Dependable and permanent tissue tube sealing

The apparatus described in this report was designed to satisfy as nearly as possible these requirements. Comparable results may be readily attained with use of glass equipment; however, the advantages of a nonbreakable apparatus are readily apparent. The utilization of liquid air or nitrogen in the condensers will shorten the drying period only a minor degree.[22] In the situation obtaining in this laboratory, dry ice has proved more economical to procure and store. The use of "O" rings to obtain glass to metal vacuum seals has proved a valuable application of this widely used industrial principle.

Sterilization of vessel segments taken at the time of routine autopsy may be performed by one of several methods.* Using adequate precautionary measures directed toward the explosive hazard, we have found the ethylene oxide technique to be reliable and simple in performance. Other than the formation of chlorohydrin compounds,† this agent probably alters little if at all the donor tissue proteins.

The method of tissue tube sealing was arrived at after trying many different techniques. Inasmuch as narrowing of the wide bore tubes is accomplished at atmospheric pressure, there has been no difficulty with delayed cracking of the glass seals. The procedure described lends itself to sealing in either a dry nitrogen atmosphere at ambient pressures or in a vacuum. A series of final dry-weight moisture determinations on human aortic tissue processed by this technique for a period of 24 hours has demonstrated residual moisture contents of 0.2% to 2.5%. These determinations were made using the method of drying to a constant weight in a vacuum oven, as well as by drying over phosphorus pentoxide.

The experimental use of freeze-dried arterial homotransplants processed by this technique has proved to be satisfactory in this

* References 14 and 26.

† Perkins, J. J., American Sterilizer Company, personal communication with the author.

laboratory during an observation period of more than two and one-half years. These results and those obtained with the clinical employment of 30 human freeze-dried arterial homotransplants will constitute the subjects of separate reports.

SUMMARY

A metal apparatus for freeze-drying arterial tissue is described and illustrated.

A freeze-drying technique utilizing this equipment is presented which allows processing routine autopsy material to a satisfactorily low residual moisture content in approximately 24 hours. Sterilization is accomplished by the use of ethylene oxide.

A new tissue-tube-sealing technique is described.

Mr. J. Walters and Mr. C. Hicks, of the College of Medicine physiopharmacology shops provided the fabrication, and Prof. J. Jacobs, Department of Physics, State University of Iowa, assisted in the designing of the technical equipment.

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Fat Embolism

An Analysis of Four Fatal Cases

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and
COL. WARNER F. BOWERS (MC), U. S. Army

INTRODUCTION

Despite the controversy over the existence and mechanism of occurrence of fat embolism, the clinical and pathological evidence in support of this entity appears conclusive. Fat embolism occurs more frequently in all types of injury than is generally recognized, and with the increase of highway accidents and the threat of mass trauma its incidence may be expected to increase. Surveys of consecutive trauma cases [7] and unselected autopsies [2] have shown that in a high percentage of trauma cases fat globules can be demonstrated in the urine and viscera on microscopic examination. In many of these cases clinical manifestations directly attributable to fat embolism are minimal or absent, whereas in others massive involvement produces a fulminating pulmonary-cerebral complex with a high mortality.

Fat embolism is so easily overlooked by the clinician or pathologist that its possibility must be kept in mind,[13] else the correct diagnosis will be missed. Ideally, a clear understanding of the pathology and pathogenesis is essential to assist in preventing its occurrence and diagnosing its presence, and to determine more accurately its prognosis. Unfortunately, such an understanding has yet to be reached, despite numerous articles on the subject, the cumulative experience of numerous cases, and wide experimental interest in this field.

The most important step leading to the diagnosis of fat embolism in trauma cases with unexplained manifestations is an awareness of the condition. A survey of microfilm records at Brooke Army Hospital over a seven year period to July, 1954, failed to reveal a single case diagnosed clinically or at autopsy. Yet during a brief period from October, 1954, to May, 1955, with interest stimulated by one case, four cases of unmistakable fat embolism were encountered. Three of these cases were diagnosed clinically before death by finding fat globules in the urine, and one case was diagnosed at autopsy.

These four cases were remarkably similar in their clinical and pathological findings. Each patient sustained fractures and soft-tissue injury as a result of an automobile accident and within a five-day period manifested severe respiratory and cerebral symptoms and died. Analysis of these cases and other reports of fatal cases * has led us to believe that in those cases with such major involvement a characteristic clinical pattern can be recognized (Table 2, *A*). In many cases with such a pattern the diagnosis can be proved clinically by a careful search for certain corroborative findings (Table 2, *B*).

REPORT OF CASES

CASE 1.—A 21-year-old Air Force private was admitted to Brooke Army Hospital on Oct. 18, 1954, after being injured in an automobile accident five hours earlier. He sustained fractures of the left femur, right tibia, and right ulna and a lacerated wound of the left ankle.

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From the General Surgery Service, Brooke Army Hospital, Fort Sam Houston, Texas (Major Nelson); Chief, Department of Surgery, and Chief, General Surgery Service, Brooke Army Hospital; Chief of Clinical Surgery, Medical Field Service School; Surgical Consultant, Fourth Army Headquarters, and Professor of Surgery, Graduate School, Baylor University (Colonel Bowers).

* References 6, 9, and 14.

Examination.—Temperature 99 F, pulse rate 84, respirations 24, and blood pressure 126/76. The patient was alert and readily answered questions, but he was somewhat confused. Other than swelling and tenderness at the various fracture sites, multiple abrasions of the forehead and face, and the lacerated wound at the left ankle, the physical and neurological examinations were normal.

Laboratory Examinations.—Leucocyte count 23,800, with 87% polymorphonuclear leucocytes. Hemoglobin 15 gm/100 cc. Urinalysis normal. Roentgenograms revealed the fractures in the midportions of the left femur, right tibia, and right ulna. Views of the skull and chest were interpreted as normal.

Course.—On the day of admission, open reduction of the fractures of the left femur and right tibia was performed. The patient left the operating room in good condition. Twenty-four hours later he became restless, apprehensive, and, later, unresponsive to questions and only partially responsive to stimuli. The blood pressure became labile, ranging from 112/72 to 156/90, and the pulse varied from 110 to 130 per minute. Neurological examination revealed the pupils to react normally and there were no abnormal changes in the reflexes. There were, however, small retinal hemorrhages and exudates bilaterally. The respiratory rate increased to as high as 80 to 100 per minute and became markedly irregular. Tracheotomy was performed. Chest roentgenograms now showed patchy areas of infiltration throughout both lung fields. Although there were no focal neurological signs, the extreme lability of the vital signs and the loss of consciousness prompted the neurosurgeon to perform bilateral trephinations on Oct. 21. No epidural, subdural, or intracerebral hematoma was found.

The diagnosis of fat embolus was suggested and confirmed by the finding of fat globules in the urine. Examination of the tracheal secretions did not reveal fat.

The patient became deeply comatose and his condition remained unimproved, despite all resuscitative efforts until his death on Oct. 23, five days after the accident.

CASE 2.—A 24-year-old veteran was admitted to Brooke Army Hospital on Dec. 6, 1954, after being injured in an automobile accident 36 hours earlier. He sustained a fracture of the right femur and multiple rib fractures bilaterally. Emergency treatment was given at a nearby hospital and, after improvement in his condition, he was transferred here.

Examination.—Temperature 101 F, pulse rate 120, respirations 30, and blood pressure 160/110. The patient was coherent but responded poorly to questions and was not well oriented. Neurological examination was otherwise normal. Borderline cyanosis was noted. There were paradoxical motion of the left anterior chest on respiration and subcutaneous crepitus of the left upper chest and neck. Breath sounds were impaired over the left lower lung field, and there were coarse rhonchi scattered throughout the left chest. There was an evident deformity of the right thigh at the fracture site.

Laboratory Examinations.—Leucocyte count 19,200, with 89% polymorphonuclear leucocytes. Hemoglobin 15.2 gm/100 cc. and hematocrit 42%. Urinalysis showed numerous granular casts per high-power field. No fat globules were noted on this examination. Chest roentgenograms revealed fractures anteriorly of ribs one through nine on the left and anterior and laterally placed fractures of ribs four through eight on the right. Both lung fields showed patchy areas of infiltration throughout (Fig. 8). Mediastinal and subcutaneous emphysema were seen. Daily roentgenograms of the chest showed little improvement in the scattered infiltrations.

Course.—Because of respiratory distress, tracheotomy and bilateral intercostal nerve blocks were performed and oxygen was administered. Only minor improvement resulted, and the patient continued to be cyanotic despite these measures. Traction was placed on the sternum, although the flail motion of the left chest was greatly diminished after tracheotomy. Under local anesthesia a Kirschner wire was placed through the upper tibia, and the right leg was placed in balanced traction.

The day after admission, fat globules were found on examination of the urine.

The blood pressure ranged from 120/90 to 190/130 and the pulse remained rapid and variable, from 120 to 160 per minute. The patient became comatose on the evening of the day following admission and died early the next morning, on Dec. 8, 1954, four days after the accident.

CASE 3.—A 20-year-old Marine Corps private was admitted to Brooke Army Hospital on Dec. 12, 1954, after being injured in an automobile accident four hours earlier. He sustained fractures of the right femur and left clavicle.

Examination.—Temperature 99 F, pulse rate 110, respirations 32, and blood pressure 130/60. The patient was lethargic but able to answer questions and follow instructions. There were swellings and tenderness at both fracture sites. Examination of the heart, lungs, and abdomen was normal. There was no external evidence of head injury. Neurological examination was normal except for questionable weakness of the right grip.

Laboratory Examinations.—Leucocyte count 19,050, with 72% polymorphonuclear leucocytes. Hemoglobin 13.0 gm/100 cc. Urinalysis revealed 1+ albumin and numerous red blood cells per high-power field. No fat globules were seen on this

examination. Chest roentgenograms showed patchy atelectasis of both lung fields.

Course.—A Kirschner wire was placed through the distal femur, and the right leg was placed in balanced traction. The patient continued to be lethargic but was well oriented and answered questions readily. There was slight cyanosis and a rapid respiratory rate. On the evening of admission, the patient became more alert and the cyanosis disappeared with the administration of nasal oxygen. The following day improvement was maintained, but the respiratory rate continued to be from 36 to 40 per minute, and the pulse rate was from 110 to 130 per minute. Later the patient became drowsy and cyanotic despite oxygen therapy and was incontinent of urine on two occasions. Neurological examination still showed no focal signs of intracranial damage. By the following morning, Dec. 14, the patient was much worse. He had vomited three times and had coughed up approximately ½ oz. of bright red blood. Because of continued respiratory distress and episodes of cyanosis, tracheotomy was performed. One hundred fifty milliliters of pink, diluted blood with a greasy consistency was aspirated. Fat globules were found in the tracheal secretions and the urine at this time. Blood pressure was 180/100, pulse rate 150, and respirations 50-60 per minute. Two hours after the tracheotomy, the patient became deeply comatose and died shortly thereafter, two days after the accident.

CASE 4.—A 25-year-old veteran was admitted to Brooke Army Hospital on April 21, 1955, after being injured in an automobile accident two hours earlier. He sustained fractures in two places, of ribs one through six on the left and fractures of the left clavicle and scapula, and a laceration of the scalp. There was no loss of consciousness. The patient was alert after the accident and gave the ambulance driver instructions concerning his personal effects.

Examination.—Blood pressure on arrival at the emergency room was 90/60, and pulse rate was 110 per minute. He was given 1000 ml. of dextran, and on arrival at the surgical ward the blood pressure was 120/74 and the pulse rate 94 per minute. There was crepitation and swelling about the left shoulder and the left upper chest. The patient had moderate respiratory distress ,and the respiratory rate was 36 per minute. There was slight paradoxical motion of the upper left chest wall anteriorly. On auscultation, there were many fine and coarse rhonchi in the left lung field. The remainder of the physical examination, including neurological examination, was normal.

Laboratory Examinations.—Leucocyte count 12,650, with 82% polymorphonuclear leukocytes. Urinalysis normal. Chest roentgenograms showed the fractures of the ribs, clavicle, and scapula on the left. There was a moderate-sized area of infiltration in the left midlung field surrounded by areas of patchy infiltration. The right lung field was clear.

Course.—Tracheotomy was done immediately because of the "wet lung" on the left and paradoxical motion of the left chest, with associated respiratory distress. Immediate improvement was noted. The paradox virtually ceased, and after aspiration of secretions through the tracheotomy, the respiratory distress was markedly diminished. Improvement progressed until 30 hours later, when, on April 22, the patient had a generalized convulsion lasting one minute. Examination following this revealed the fundi to be normal; abdominal reflexes were absent, and there was an abnormal plantar reflex bilaterally. The urine and tracheal secretions were examined for fat globules, but none were found. The vital signs began to undergo marked fluctuations, and the patient became semicomatose. Despite the absence of any localizing neurological signs, bilateral trephinations were performed. A small (30 ml.) hematoma was evacuated from the subdural space on the right. During the procedure, the patient had two additional generalized convulsions and lapsed into a deep coma from which he never recovered, and he died 12 hours later, 52 hours after the accident.

OBSERVATIONS

Clinical Findings.—The pertinent clinical findings in our four cases are presented in Table 1. Only in Case 2 were the injuries considered to be of sufficient severity to have produced death in the absence of fat embolism. In this case 36 hours had elapsed before admission and it was believed in retrospect that manifestations of fat embolism were already present on admission. This patient was less well oriented than the others and had a greater degree of respiratory difficulty, although the multiple fractured ribs certainly accounted, to a large degree, for this. In every case the initial response to resuscitative measures was considered to be satisfactory. The later development of a severe pulmonary-cerebral complex was, in general, unexpected. Once these manifestations were present, improvement never occurred, despite vigorous therapeutic efforts. In Cases 1, 2, and 3 fat was found in the urine, not on the initial examination, but only after repeat studies. In Case 4 the diagnosis of fat embolism was suspected before death, but clinical or laboratory confirmation

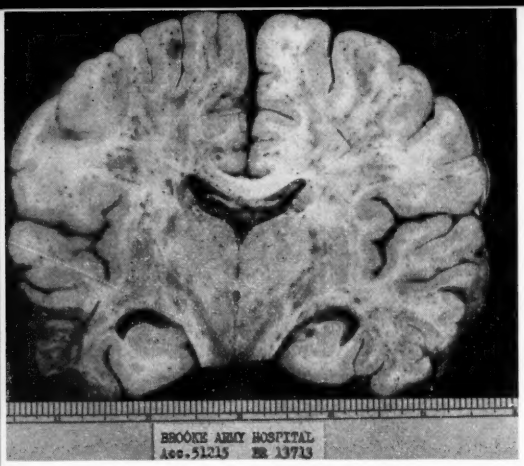


Fig. 1 (Case 2).—Brain showing multiple petechial hemorrhages on cut surface. Note the greater involvement of the white matter.

could not be obtained. In Cases 2 and 4 tracheotomy markedly reduced the amount of paradoxical or flail motion of the thorax from the rib fractures. However, in all cases respiratory distress, and even cyanosis, persisted in spite of oxygen therapy, and tracheal secretions were a problem, despite frequent aspirations. The remarkable similarity of these cases to each other and to other reported cases makes us agree with Newman [9] that earlier conclusions by Scuderi [12] regarding the inconclusiveness of the clinical findings is, in general, too pessimistic.

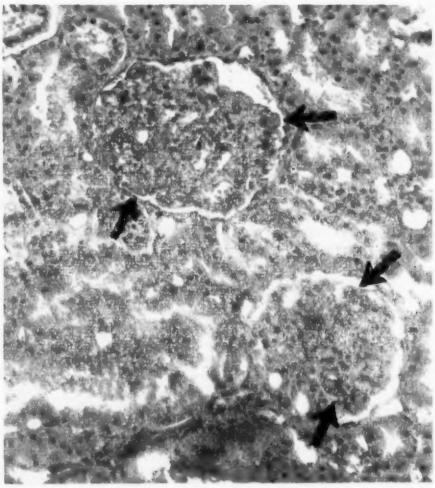
Pathological Findings.—The principal pathological findings, other than the injuries already mentioned, were alike in all four cases. The organs chiefly involved were the lungs, brain, and kidneys. There was inconstant involvement of the other viscera—liver, spleen, pancreas, and myocardial vessels—in the four cases.

Grossly, in each case there was intense congestion and edema of the lungs and brain. The brain on cut surface showed many petechial hemorrhages, more frequent in the white matter than the gray matter (Fig. 1). In one case the lung on cut surface exuded oily droplets. The kidneys, although microscopically involved, showed no gross abnormalities on cut surface.

Microscopically, the presence of fat emboli in the small arterioles and capillaries was demonstrated by Sudan IV stain, using frozen section technique. The presence of fat emboli on ordinary stained paraffin sections may be suspected from the presence of

Fig. 2 (Case 1).—Kidney, paraffin section. Note the large vacuoles in the glomerulus which should lead to suspicion of fat embolus when ordinary paraffin sections are examined. Hematoxylin and eosin stain; × 475.

Fig. 3 (Case 3).—Kidney, frozen section. Fat globules are seen in the glomerular vessels (arrows). Sudan IV stain; × 105.



vacuoles within the capillaries.[14] These changes are best demonstrated in the lungs and kidneys (Fig. 2) but have also been described in the choroid plexuses by Russell and by Silverstein.[13] With fat stains plugging of the afferent arterioles and capillaries of the glomerular tufts was easily demonstrated in all cases (Fig. 3). In the three cases with lipuria fat globules were also found in

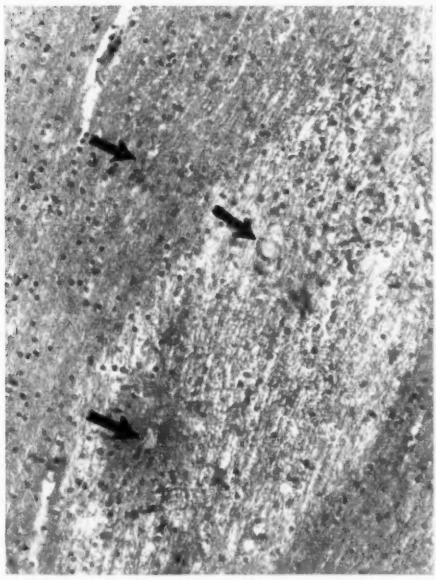


Fig. 4 (Case 1).—Brain, frozen section. Fat globules in the cerebral capillaries (arrows). Note the anemic infarct surrounding the area containing two of the emboli. Sudan IV stain; × 105.

the collecting tubules. In the brain the gross petechiae were represented microscopically by small foci of perivascular hemorrhage and degeneration. In some areas adjacent to an occluded vessel, there were small anemic infarcts (Fig. 4). There was also minimal polymorphonuclear and lymphocytic infiltration surrounding the areas of occlusion. In the lungs plugging of both alveolar capillaries (Fig. 5) and pulmonary arterioles (Fig. 6) was found. Extensive hyperemia and edema were very evident. There was also polymorphonuclear infiltration, and in two cases

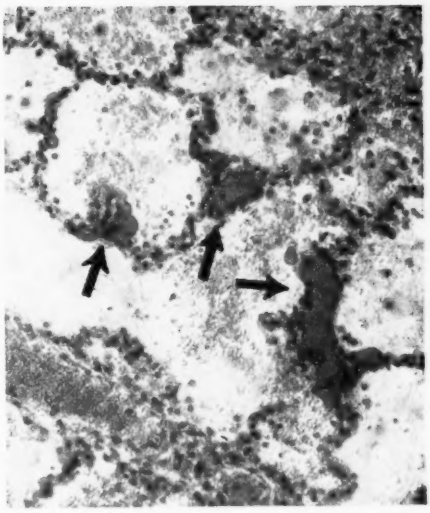
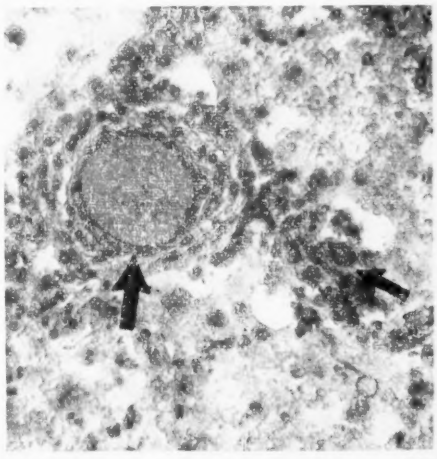


Fig. 5 (Case 3).—Lung, frozen section. Fat globules (arrows) in pulmonary and alveolar vessels. Sudan IV stain; × 105.

mononuclear phagocytes contained fat. There was little evidence microscopically to determine whether the harmful action was due to simple occlusion or to a toxic action on the vessel wall. Stains for neutral fat were not done.

Fig. 6 (Case 3).—Lung, frozen section. Fat is seen in both large and small pulmonary vessels (arrows). Sudan IV stain; × 475.



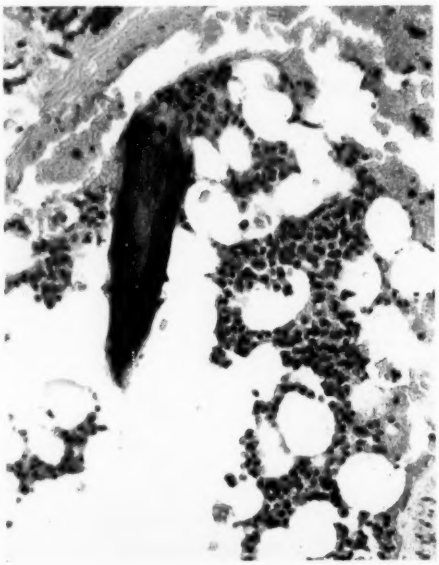
COMMENT

Incidence and Occurrence.—Since many cases are probably missed clinically and pathologically, the true incidence of fat embolism is difficult to determine. Many times death in these cases is ascribed to secondary shock, pulmonary edema, pneumonia, cerebral injury, or idiosyncracy to an anesthetic agent or drug.[9] Denman and Gragg [2] observed that the incidence of fat embolism approaches that of thrombotic embolism, and they believe that the condition is deserving of more attention clinically. They found 7% of autopsies selected at random to have fat embolism of sufficient severity to account for death in previously undiagnosed cases.

Fat embolism is most commonly found in trauma cases, especially those with massive soft-tissue injury and fractures of the long bones. Vance [15] found fat embolism as a complication in 75% of fractures of long bones and a significant factor in the death of 20% of his 246 cases. Warren,[14] reporting 100 cases, found fractures in 91% and fractures of the femur or tibia in 82%. In 80 fatal cases compiled at the 406th Medical Laboratory,[5] the severity and types of trauma were correlated with the presence and severity of fat embolism. There was no strict correlation with the amount of osseous damage, but there was some relation between the severity of the injury as a whole and the number of emboli and organs involved. Fat embolism was found to be common in vehicular accidents and beatings with massive soft-tissue damage. The kidney was the organ most frequently involved, and it was interesting to note that in no case where the cerebrum was involved was the kidney spared. Peltier [10] concluded that fatty emboli are by and large normal sequelae of osseous injury and become of pathological significance when associated with factors as yet unrecognized. Fat embolism has a high incidence in lipectomy where a "fatty apron" is removed from the abdominal wall,† and it has been found in association with laparotomy in obese patients [11] thoracotomy,[1] and orthopedic procedures.[10] It is occasionally mentioned in association with instillation of oil into body cavities, poisonings, and burns.

Pathogenesis and Pathologic Physiology.—There is general agreement that the essentials for entry of embolic fat into the circulation are mobilized fat, patent disrupted veins, and local pressure.[14] The experimental work of Busch, who in 1866 demonstrated the passage of dye from the medullary cavity of fractured bones to the pulmonary vessels, conclusively demonstrated that an embolic process can result from a fracture. Further proof that embolism does occur is the occasional finding of bone marrow or even spicules of bone in the pulmonary vessels after fractures. In one case at Brooke Army Hospital, not in the group under present consideration, both bone marrow and a spicule of bone were found in the pulmonary vessels at autopsy (Fig. 7). The patient died almost immediately of severe injuries following an automobile accident.

Fig. 7.—Lung, paraffin section. Convincing proof that embolism from a fracture site can occur is shown by the presence of a bone spicule and bone marrow in a pulmonary vessel. Autopsy finding in a young soldier who sustained fatal injuries in an automobile accident. Hematoxylin and eosin stain; × 105.



† Bowers, W. F.: Personal data.

There is less agreement concerning the source and amount of fat necessary to produce symptoms or cause death. Evidence has been advanced to show that the amount of fat available from the medullary cavity of a femur is less than the amount calculated necessary to cause symptoms or death.[8] The amount necessary to cause death in humans has been variously estimated up to 120 ml.,[8] but, since this figure is based on interpolation from animal experiments, its accuracy might be open to question. Fat embolism also occurs in cases of trivial injury, fractures of non-fat-bearing bones—the patella or facial bones—and in poisonings or septicemia where there is no obvious source for the fat. These discrepancies in the source and amount of fat necessary to cause symptoms have led to alternative theories to explain the pathologic effects. The mechanisms suggested are (1) chemical changes in the blood which cause demulsification and coalescence of the serum lipids into globules of sufficient size to produce obstruction, (2) destruction of the normal emulsoid state of the serum lipids by a "salting-out" process from the presence of abnormal fat, and (3) hydrolysis of the fat with toxic action due to release of fatty acids. Unfortunately, none of these observations as yet has been fully substantiated clinically or experimentally.

Death from fat embolism is due primarily to blockage of vessels in the lungs and brain. The liver, spleen, pancreas, and kidney are able to withstand the effects of fatty blockage without recognizable alterations of function. This may be due to the reserve capacity of these organs as compared with that of the brain and to a reduction in the number of emboli reaching these organs after filtration in the lungs, which bears the brunt of the embolic insult. Although it seems plausible that blockage of the coronary circulation and myocardial damage would be a significant factor in the mortality, few clinical or pathological reports have made mention of this. Certainly, the effects of myocardial damage are overshadowed by the pulmonary and cerebral manifestations and may be present without being noticed. It does not seem likely that the alterations of pulse and eventual failure of circulation can be directly attributable to cardiac damage, since the heart shows no evidence of true infarction, as seen in thrombotic occlusion of the coronary vessels. The occasional finding of right ventricular dilatation at autopsy more likely reflects alterations of the pulmonary dynamics, rather than any specific effects on the myocardium.

Diagnosis.—Fat embolism is most frequently overlooked because it is not considered as a diagnostic possibility. The pertinent clinical findings in our four cases are summarized in Table 1 and a tabulation of important diagnostic factors is given in Table 2.

In cases with minimal involvement mild elevations of temperature, pulse rate, and respiration, apprehension, irritability, and mental confusion frequently are considered as being due to other causes. The effects are often transient, and complete recovery is the rule.

In cases with major involvement the clinical findings usually follow the pattern as outlined in part A, Table 2. A high index of suspicion should be raised when any of these manifestations take place in the injured patient. Respiratory or cerebral abnormalities may be evidenced alone, but more frequently a combination of the two is present.[4] Theoretically, respiratory symptoms should precede cerebral symptoms, but this also is not necessarily so. Possibly some of the early cerebral findings are in reality expressions of anoxia secondary to the respiratory insult.

It is of importance to recognize the chronological order of the history, with trauma first, next, a "free" period or period of improvement, and, later, the development of the severe pulmonary-cerebral complex. In each of our cases this sequence of symptoms was quite apparent, and there was a period of definite improvement before signs of fat embolism occurred. The average time elapsed after the accident before the onset of symptoms was 36 hours, with a range of 30 to 44 hours in the four patients. In general, if this period is short and the early symptoms

TABLE 1.—*Clinical Findings in Four Fatal Cases of Fat Embolism*

Case No.	Injury	Vital Signs on Admission	Maximum Abnormality in Vital Signs	Time Interval Accident→Death (Days)	Chest Roentgenograms	Laboratory Examinations for Fat Globules		Petechiae Skin	Fundi
						Urine	Sputum		
1	Fractures Left femur Left tibia Right ulna Laceration Left ankle Abrasions Face & head	B. P. 126/76 Pulse 84 Resp. 24 Temp. 99 F	B. P. 156/90 Pulse 130 Resp. 80-100 Temp. 103 F	5	Patchy atelectasis, bilateral	+	0	0	Changes consistent with fat embolism
2	Fractures Right femur Ribs 1-9 left 4-8 right	B. P. 160/100 Pulse 120 Resp. 30 Temp. 101 F	B. P. 190/130 Pulse 160 Resp. 50 Temp. 101.8 F	4	Patchy atelectasis, bilateral	+	0	0	Normal
3	Fractures Right femur Left clavicle 4th rib, right	B. P. 130/60 Pulse 110 Resp. 32 Temp. 99 F	B. P. 180/100 Pulse 150 Resp. 50 Temp. 101 F	2	Patchy atelectasis, bilateral	+	+	0	Normal
4	Fractures Ribs, 1-6 left Left scapula Left clavicle Laceration Scalp	B. P. 90/60 Pulse 110 Resp. 36 Temp. 100 F	B. P. 140/98 Pulse 120 Resp. 40 Temp. 101 F	2	Patchy infiltration, left lung	0	0	0	Normal

severe, the prognosis is grave. An additional factor of diagnostic importance is that once severe manifestations are present, all therapeutic endeavors fail to produce the desired response.

Roentgenograms of the chest, in our experience, are a valuable adjunct in diagnosing fat embolism. In all four cases the appearance was similar to that seen in Case 2, (Fig. 8) which showed the severest changes. In Cases 1 and 3, in which there had been no chest injury, there were more changes than Case 4, in which fractures of the ribs, scapula, and clavicle were present. The common finding is a patchy infiltration, usually of both lung fields, which generally resembles the appearance of pulmonary edema, except that involvement of the upper and lower lung

TABLE 2.—*The Syndrome of Fat Embolism*

A. Suggestive Findings
   1. Trauma
   2. Adequate response to initial resuscitative measures and a period of improvement
   3. Absence of sufficient pulmonary or cerebral injury to account for later manifestations
   4. Normal neurological examination, initially
   5. Later, severe neurological changes, particularly alterations of the conscious state without definite localizing signs or signs of increased intracranial pressure
   6. Marked abnormalities and fluctuations of the vital signs, i. e., pulse, temperature, respirations, and blood pressure
   7. Dyspnea, cyanosis and marked increase and irregularity of respirations, "wet lung"
   8. Failure of the respiratory distress to respond adequately to oxygen, tracheotomy, intercostal nerve block of fractured ribs, and inability to clear tracheobronchial secretions completely by suction
   9. Patchy infiltration of one or both lung fields on roentgenograms

B. Diagnostic Findings
   1. Petechiae of the skin, especially the upper torso, neck, and conjunctiva
   2. Retinal changes
   3. Fat globules in the urine

Fig. 8 (Case 2).—Chest roentgenogram. Note the widespread patchy infiltration occupying both lung fields. Mediastinal and subcutaneous emphysema are also present.

fields is equal, or bronchopneumonia, except that the involvement is too widespread.

Once these diagnostic factors are recognized and fat embolism is suspected, it is important to search for confirmatory signs to prove the diagnosis (Table 2, B). The most important of these are (1) petechiae of the skin, especially of the upper torso and neck; (2) petechiae of the conjunctiva and retina and other retinal changes, and (3) fat in the urine.

Petechiae of the skin and conjunctiva were not found in any of our cases, possibly because a diligent search was not made, except in Case 4, the only case in which fat globules were not found in the urine. Retinal changes consistent with fat embolism ‡ were seen in Case 1, and questionable changes were found in Case 3. The fundi were repeatedly examined in all four cases.

The presence of fat in the urine in three cases agrees with the findings of the 406th Medical Laboratory in Japan that the kidney is the most consistently involved organ.[5] In one case fat globules were found only after examination of the last portion of the urine specimen. The importance of a careful collection of all the urine has been stressed by Scuderi.[12] Examination of the serum, sputum, or gastric secretions for fat is much less reliable than examination of the urine. Peltier [10] has described identification of fat in the serum with use of a fluorochrome dye. We have had no experience with this method.

Differential Diagnosis.—Fat embolism is most commonly confused with the other effects of trauma, such as from head or chest injury, blast injury, and crush syndrome and secondary shock. It may also be mistaken for certain diseases, such as septicemia, diabetes, and fulminating pneumonitis, and for a variety of miscellaneous conditions, including air embolism, complications of anesthesia, drug poisoning or idiosyncrasy, heat exhaustion, and delerium tremens. Since fat embolism may occur in association with many of the above conditions, the distinction may be difficult indeed. In the presence of trauma the possible effects of chest and cerebral injuries cause the greatest difficulty.

Fortunately, in chest injuries physical examination and chest roentgenograms furnish an efficient means for determining the presence and degree of impairment of pulmonary function. In most instances a favorable response can be obtained by the aspiration of abnormal fluids and air, relief of pain by nerve block, and tracheotomy to improve ventilatory efficiency and remove accumulated secretions. When these measures do not produce the desired response, other causes for the continued symptoms, such as fat embolism, must be considered.

With head injuries the means for determining the pathological state are less exact, and frequently exploratory craniotomy must be performed because of an altered state of consciousness and abnormal vital signs, in the absence of focal neurological changes. Many times, then, the findings may be identical with those due to fat embolism.[13] This similarity and the frequent association of fat embolism with head injury make the decision not to perform exploratory trephination a difficult one indeed. In Cases 1 and 4 cranial exploration was performed despite the absence of focal neurological changes. A small subdural hematoma, of less than 30 ml. diameter, was found in Case 4 but was not considered to be clinically significant. In neither case at the time of exploration had fat been found in the urine. In Cases 2 and 3 the finding of lipuria influenced our decision not to operate until more definite signs of a specific intracranial lesion were present.

Treatment.—Although treatment is far from satisfactory because the disease so often remains unrecognized, even when we had proof of the diagnosis we were unable to reverse the progressive deterioration in these patients. Nevertheless, we believe that an attitude of hopelessness should not be the rule, and vigorous supportive efforts should be made, since the chance of recovery is increased each day that the patient remains alive. A definite decrease in mortality was found in those patients who survived longer

‡ References 3 and 9.

than six days.§ Although the mortality is more related to the degree of embolism, the kidneys and liver may help by the excretion and metabolism of fat.

The most important measures are the maintenance of an adequate blood volume, hydration, and oxygenation. Shock should be corrected early, and respiratory physiology should be restored to as near normal as possible. High concentrations of oxygen have been found to be very beneficial.[4] Other measures have been advocated, such as intravenous demulsifying agents, insulin to assist the liver to metabolize the fat, ligation of leg veins to block further emboli, and stellate ganglion block to increase cerebral circulation. The experiences with these methods are limited and the results uncertain at the present time.

SUMMARY

Four similar cases of fatal fat embolism are presented, with emphasis on the clinical and pathological findings.

The diagnosis of fat embolism is often missed because of the uncertain nature of the disease in its milder forms and because of a lack of awareness of the attending physician.

Analysis of our four cases and cases from other reports reveals a rather characteristic clinical pattern, from which the diagnosis may be suspected.

We were able to establish a positive diagnosis in three of our four cases by finding fat in the urine. In those cases where laboratory proof is not obtained, a diagnosis based on clinical grounds alone, especially if petechiae and retinal change are present, seems entirely plausible.

Despite the fact that there is no satisfactory treatment for fat embolism and the mortality is chiefly related to the degree of embolization, vigorous supportive measures should be employed to salvage those patients who might otherwise be lost.

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Anterior Transthoracic Approach for Upper Thoracic Sympathectomy

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INTRODUCTION

The most commonly employed surgical approach for a sympathectomy for the upper extremity or for relief of angina pectoris with or without coronary insufficiency is the posterior extrapleural operation of the Smithwick type, or its modification. For sympathetic denervation of the upper extremity by this technique, a resection of a short posterior section of the third rib was accomplished with the patient in a face-down position. A portion of the second and third intercostal nerves was resected, the rami communicantes or the sympathetic chain at these levels were divided, and the sympathetic chain was likewise divided below the third sympathetic ganglion, whereas, the denervation of the heart required a more extensive resection of the upper sympathetic chain.

This former posterior approach had its many pitfalls and limitations, which were mainly technical. The degree and type of exposure were usually inadequate, imposing many obstacles, particularly of performance of an operation which might result in an incomplete denervation, or, in the event a vessel was inadvertently opened, it would be difficult to control the bleeding. Also, variations in the anatomy, particularly those associated with the sympathetic nervous system in this area, are not easily visualized and recognized by this approach, thereby resulting in an incomplete denervation; this pertains particularly to the pathways to the upper extremity. A Smithwick procedure, or its modification, precludes the ablation of the sympathetic pathways to the upper extremity which pass via the first thoracic rami to the first thoracic nerve—this occurs in about 10% to 15% of the cases—or the pathways which arise from the fourth or fifth thoracic level of the cord and pass out of the chain at these levels or at a higher level.

The face-down position of the patient in a posterior surgical approach is not a satisfactory or an entirely safe position from the standpoint of administration of anesthetics. The cardiac patient, generally speaking, does poorly in this position, and this is a handicap which may increase both the morbidity and the mortality rates, primarily in those patients being operated upon for the relief of angina pectoris, coronary insufficiency, and/or status anginosus.

Stellate ganglionectomy for the relief of angina pectoris and/or coronary insufficiency has proved to be an entirely unsatisfactory and inadequate procedure. This was due to an incomplete sympathetic denervation of the heart, resulting in an incomplete relief of cardiac and referred pain. This procedure likewise resulted in Horner's syndrome, which is an unsightly and undesirable sequela. Such a procedure has fallen into disrepute, and rightly so, since it resulted in only a partial relief of symptoms. It is readily apparent from our present-day knowledge of the anatomy and physiology of the sympathetic nerve supply to the heart that such a procedure would result in a high percentage of failures. The advances in the knowledge of the sympathetic supply to the heart in the human being has come through

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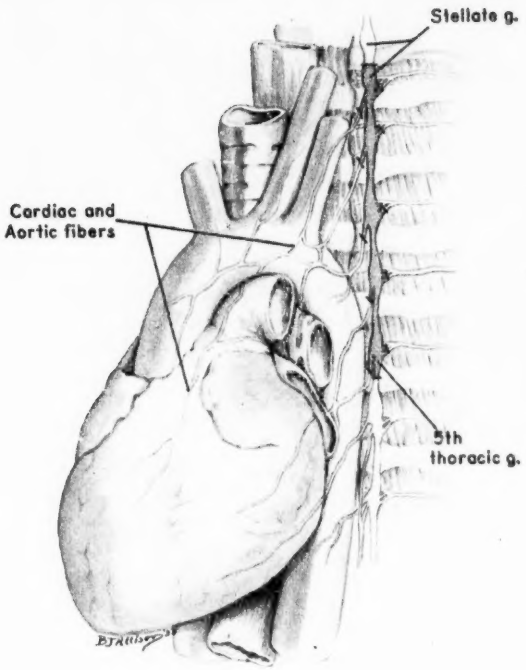

Fig. 1.—Relational anatomy of the heart, great vessels, and the sympathetic chain, ganglia, rami, and associated branches, as seen in the left thoracic exposure. The dark area of the sympathetic chain indicated the portion which is removed, and the short black bars indicate the sites where division is accomplished.

careful evaluation of the results of various surgical procedures performed upon the sympathetic division of the autonomic nervous system in the upper thoracic region.

SYMPATHETIC PATHWAYS TO HEART AND UPPER EXTREMITY (Figs. 1 and 2)

It is now fairly well established that the sympathetic innervation for the upper extremity arises from the spinal cord, usually from the second to the sixth or seventh thoracic level, and that these preganglionic neurones enter the sympathetic chain and ascend, usually leaving it (via the rami communicantes) at the second and third thoracic levels, where they join the second and third intercostal nerves. The greatest number, generally, leave at the level of the second thoracic ganglion. However, in about 10% to 15% of the cases a major sympathetic pathway may leave via the first thoracic ganglion.

The cardiac sympathetic innervation is derived bilaterally; however, clinically, the left side is more important. The preganglionic neurones arise from and leave the spinal cord from the first through the fifth thoracic segment; they synapse with postganglionic neurones at the first through the fifth thoracic ganglion. These cardiac fibers then pass directly to the heart and coronary vascular system. In addition, the preganglionic neurones arising from the spinal cord as noted above ascend in the sympathetic chain to synapse in the cervical portion of the chain at the inferior, middle, and superior cervical ganglia. From these the superior, middle, and inferior cardiac nerves (which are postganglionic neurones) pass downward in the neck to the heart. It is generally agreed that

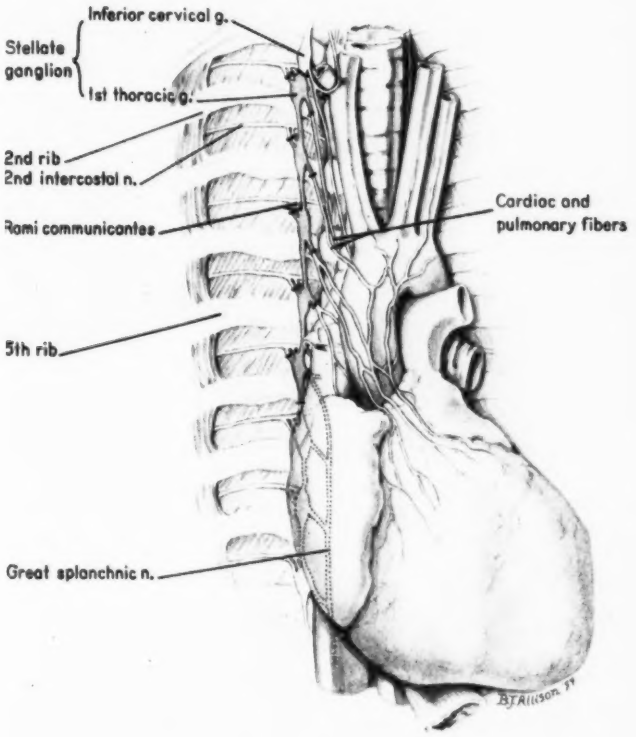

Fig. 2.—The same as Figure 1, as seen from a right thoracic exposure.

all of these pathways, possibly with the exception of the superior cervical cardiac nerve and the first thoracic sympathetic fibers, contain visceral afferent (pain) components which are responsible for conveying pain impulses from the heart and the coronary vascular tree to the central nervous system. Therefore, in order to ablate all possible visceral afferent pathways from the heart, it is necessary to remove the sympathetic chain and associated ganglia from the first through the fifth thoracic (dorsal) level. Frequently only a left-sided procedure will be necessary to relieve the patient of his distressing cardiac symptoms and referred cardiac pain, provided the pain is all left-sided, as is often the case.

PRESENT SURGICAL TECHNIQUE

The main purpose of this presentation is to present a new surgical approach to this segment of the sympathetic chain. Since April, 1953, we have performed 27 operations utilizing the technique described below.

OPERATIVE TECHNIQUE

The patient is placed upon the operating room table in the supine position with the side of the thorax to be operated on elevated about 15 degrees by a folded sheet or pad under the scapula (Fig. 3, *A*). The upper extremity is abducted to 90 degrees at the shoulder and the elbow flexed at 90 degrees, with the forearm anchored to a crossbar, as shown in Figure 3, *A*. An endotracheal anesthetic is administered.

The skin incision extends anteriorly from the parasternal line to the anterior or mid-axillary line over the third intercostal space (Fig. 3, *A*). The pectoralis major and intercostal muscles are divided and the pleura incised in the third intercostal space (Fig.

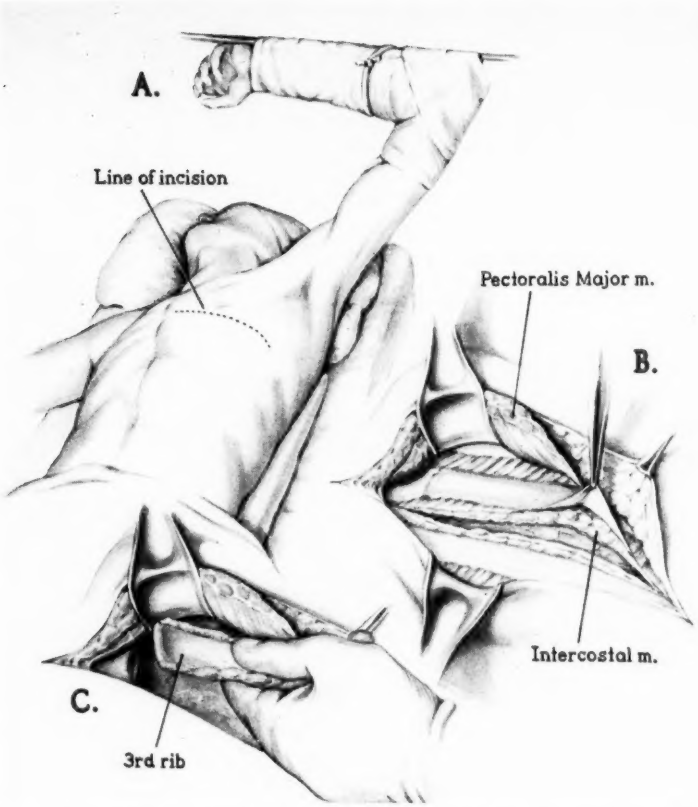

Fig. 3.—*A*, Position of patient on operating table. Dotted line represents location of skin incision below nipple. *B*, divison of the pectoralis major muscle and the intercostal muscles in the third intercostal space; the parietal pleura is also divided in the same space. *C*, the costal cartilage of the third rib anteriorly is divided vertically by scalpel to increase the wound exposure.

3, *B* and *C*). The costal cartilage of the third rib is divided with a scalpel to permit a greater exposure in the upper thoracic cage (Figs. 3, *C* and 4, *A*).

The left upper lobe (the right upper and middle lobes in a right-sided procedure) is deflated and depressed downward to permit complete exposure and visualization of the upper posterior aspect of the thoracic wall. The parietal pleura overlying the angles of the ribs posteriorly is incised from below the fifth rib to the apex of the thoracic cage. This incision and dissection of the pleura free from the chest wall is directly over the upper dorsal portion of the sympathetic trunk (Fig. 4, *B* and *C*). In fact, the sympathetic chain and ganglia can usually be visualized beneath the pleura in this area before incision is made—this is used as the guiding line for the site of incision of the pleura posteriorly (Fig. 4, *B*).

The sympathetic chain is then dissected free from the chest wall, care being practiced particularly at each intercostal space, for it is at this point that the chain, ganglion, and associated rami are in close proximity to the intercostal vessels (Fig. 4, *C*). This chain is divided below the fifth thoracic ganglion, and the dissection is carried upward until the apex of the chest cavity is reached. At this point a more careful dissection is necessary in order to avoid injury or destruc-

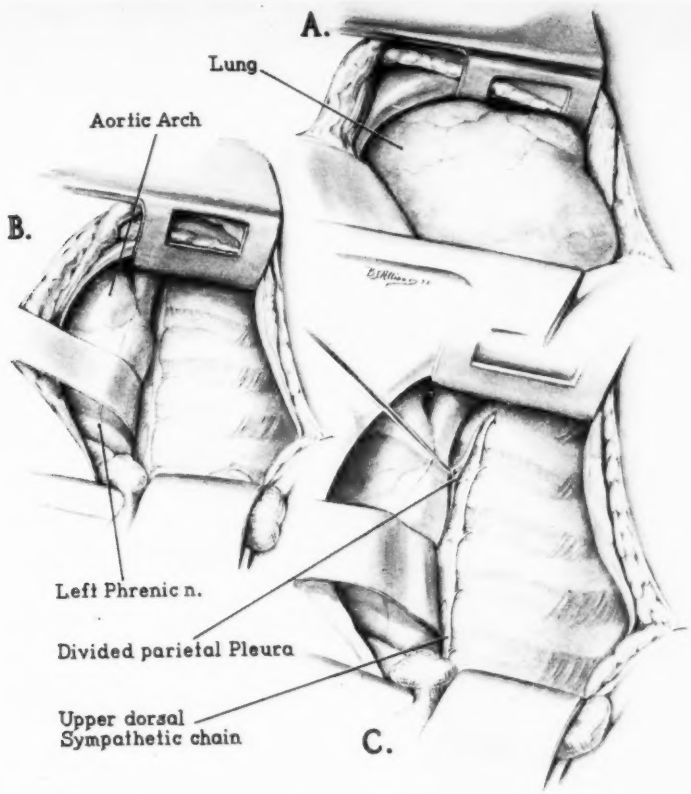

Fig. 4.—*A*, general exposure obtained after insertion of self-retaining chest retractor. *B*, special lung and cardiac retractors in place revealing the upper posterior wall of the left thorax. The sympathetic chain and associated ganglia are readily seen beneath the posterior parietal pleura. *C*, the parietal pleura posteriorly has been divided vertically directly over the sympathetic chain from the apex of the thorax to below the fifth rib. The medial branches, the ganglia, and associated rami communicantes are easily visualized. Special long-handled hooks are used to pick up the pleura to facilitate division of this structure.

tion of the ciliary pathways to the pupil, thereby averting a Horner syndrome.

In order to prevent this injury or destruction, only the lower one-third of the stellate ganglion is dissected free and partially mobilized. The dissection of this ganglion is carried to a point just cephalad to the rami going to the first thoracic nerve (Fig. 5, *A*). Since there are variations in the pattern of the sympathetics, it is important not only to count the ganglia but also to count the ribs as landmarks for the determination of the extent of the denervation. It is easy to miscount and to miss the first rib. Actually, it is represented posteriorly as a narrow structure, since its curvature and direction are different from those of the adjoining ribs below. The second rib, as well as those below, is broad and flat. The first and second ribs, likewise, are in very close proximity to one another, and the intervening intercostal space is very narrow (Fig. 5, *A*).

When the first rib is located, the first thoracic ganglion lies just beneath its angle and the rami from this ganglion are easily visualized. It is at this point that the dissection of the chain terminates. By so doing, an adequate denervation will be accomplished without destruction of the pathways to the pupil. The transection of the sympathetic

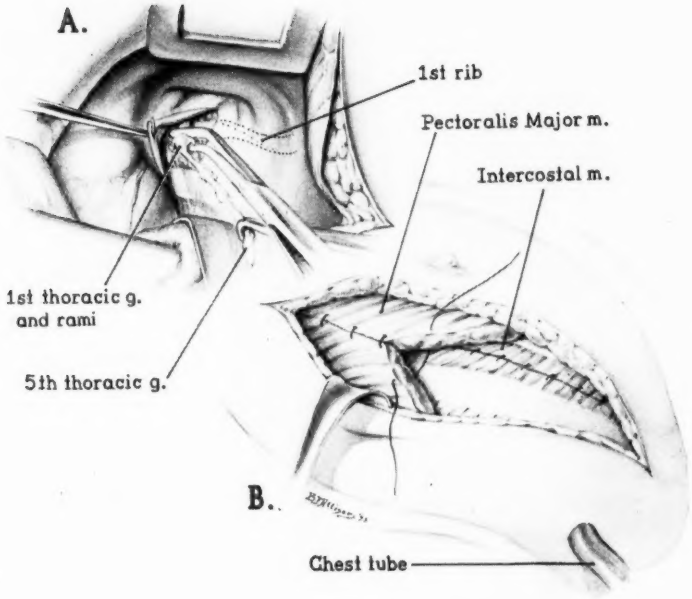

Fig. 5.—*A*, The left upper thoracic sympathetic chain and associated five ganglia have been dissected free. The dissection of the stellate ganglia is carried just cephalad to the first thoracic ramus communicans, where it is transected by a special right-angle scissors. *B*, The intercostal and pectoralis muscles are separately sutured with interrupted 00 nonabsorbable surgical (silk) sutures. The intercostal chest tube is placed through a separate anterior stab wound one or two interspaces below the intercostal incision.

chain is accomplished immediately cephalad to these first thoracic rami across the lower third of the stellate ganglion (Fig. 5, *A*). The extent of resection of the chain and associated ganglia is indicated in Figures 1 and 2.

The stellate ganglion represents a fusion of the inferior cervical ganglion with the first thoracic (dorsal) ganglion. The configuration of this structure, as well as its size, is variable. In many cases it is represented by one fusiform body of considerable length, being the shape and size of a small flat almond. In about one-third of the cases the fusion of the first thoracic ganglion to the inferior cervical ganglion is incomplete, so that the thoracic ganglion is attached to the inferior part of the inferior cervical ganglion by a short broad strand. These variations are important to the surgeon in being able to recognize the structures in this area and to ensure a satisfactory and complete denervation without producing Horner's syndrome.

After completion of the resection of the chain, the deflated lung is reexpanded under direct vision while the chest wound is closed in layers, the intercostal and the pectoralis major muscle layers being sutured separately with interrupted 00 nonabsorbable surgical (silk) sutures (Fig. 5, *B*). A small intercostal chest tube is inserted through a small stab wound in the anterior axillary line about two interspaces below the intercostal incision (Fig. 5, *B*). This is connected to an underwater-seal suction-type apparatus when the

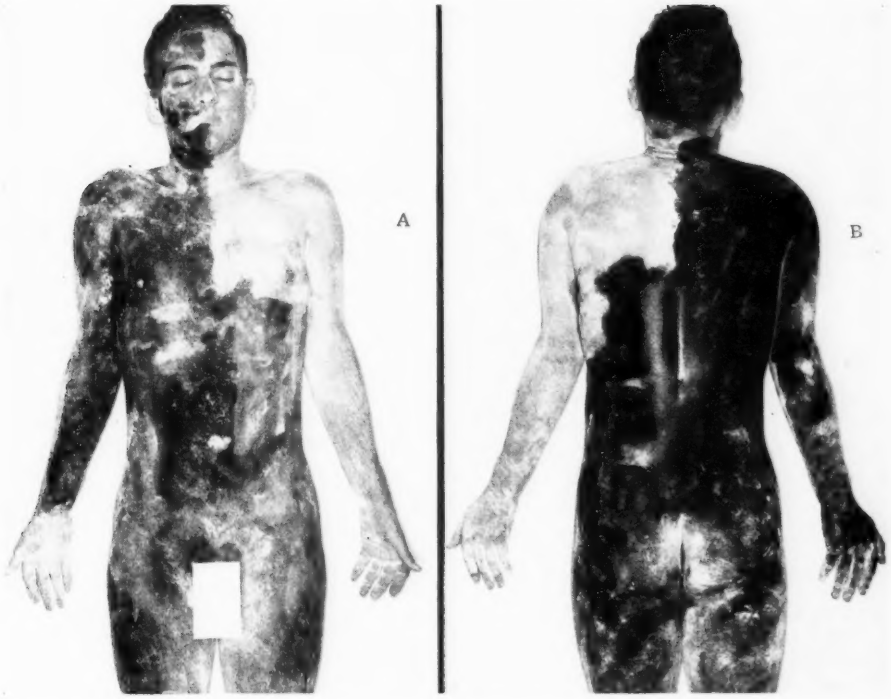

Fig. 6A.—Anterior view revealing absence of sweating on the left side of the upper chest and shoulders. There is, also, loss of sweating of the entire left upper extremity and left half of the head and neck. (The light areas represent loss of sweating.) Fig. 6B.—Posterior view, same as Figure 6A.

patient is returned to his room. The entrapped pleural air is removed via this tube during wound closure and by positive pressure expansion of the lung by the anesthetist. The subcutaneous and skin closure is accomplished with fine interrupted nonabsorbable surgical (silk) sutures. The chest tube is usually removed in 24 to 48 hours if there are no pulmonary or intrapleural complications.

The patient is ambulated the same evening or on the first postoperative day. His activities are increased daily thereafter.

RESULTS

The denervations obtained in all cases were complete and are typified by the sweating patterns shown in Figure 6, *A* and *B*. In all cases, except one, Horner's syndrome did not develop. This one exception had a bilateral denervation; however, on the left side Horner's syndrome resulted. This was due to a more extensive dissection of the stellate ganglion, which was intentional in order to demonstrate the anatomy of this area during the filming of this procedure.

MORBIDITY

The morbidity rate is definitely lower in this group than in the group of patients in whom a posterior or modified Smithwick procedure was performed. The patient experiences less discomfort following surgery and appears to have a smoother and a more rapid convalescent period. There are fewer wound and pleural complications. The cardiac patient becomes a better risk, and there is less hazard during surgery in this type of patient because of the position of the patient while under anesthesia.

COMMENT

There are innumerable advantages to this anterior transpleural approach to the sym-

pathetic denervation of the upper extremity, of the heart and of the coronary vascular tree. This technique permits a better and simpler approach to the chain, with less risk and technical hazards than the posterior approach. The surgeon can more readily visualize and, therefore, perform a more thorough operation, which will ensure a complete permanent type of denervation. This can be accomplished with greater ease and within a shorter operating time. It will permit the surgeon to do a more definitive type of denervation with a better chance to recognize and remove aberrant pathways or variations which may exist. By an adequate exposure, such as obtained by this method, a careful dissection of the lower portion of the stellate ganglion can be performed, removing the first thoracic ganglion, without producing Horner's syndrome.

It is generally stated that the pupillociliary pathways of the sympathetics for controlling pupillary dilatation arise as preganglionic neurones from the eighth cervical and/or first thoracic portion of the spinal cord and leave the cord usually via the first dorsal root to the first thoracic sympathetic ganglion via the first ramus communicans. The neurone then passes cephalad to the superior cervical ganglion, where it synapses the postganglionic neurones, and then to the muscles of the iris via the carotid vessels. If this arrangement of pathways is correct, then any procedure which would destroy the first thoracic ganglion (lower portion of the stellate) or the first ramus communicans should result in Horner's syndrome. In all the cases performed by our staff with the technique described above in which these two structures were divided and/or excised, Horner's syndrome did not occur. As a result of this, it is our contention that the origin of these pathways in the cord are correct but that they appear to gain entrance to the upper portion of the stellate ganglion via some pathway other than by the first ramus communicans. Other investigators have shown that if the upper portion of the stellate ganglion is destroyed Horner's syndrome develops. Therefore, these pathways do reach and pass through the upper portion of this ganglion via a pathway other than the first thoracic ganglia or ramus communicans.

SUMMARY AND CONCLUSIONS

A new upper anterior intercostal transpleural approach to the upper thoracic (dorsal) sympathetic chain for sympathetic denervation of the upper extremities and/or heart and its coronary vascular system is described. Since April, 1953, this procedure was performed 27 times in 20 consecutive cases, resulting in a complete sympathetic denervation of the upper extremity, head, neck and upper anterior and posterior aspects of the chest and also with a complete sympathetic denervation of all visceral efferent and afferent (pain) pathways to the heart.

This technique ensures a complete denervation with greater ease of performance for the surgeon and with a minimal risk and a smoother postoperative convalescence for the patient. The cardiac patient with or without angina pectoris and/or coronary insufficiency withstands this procedure better, and it is safer because of the position of the patient on the operating table.

This technique does not interrupt the sympathetic pupillociliary pathways and, therefore, does not result in Horner's syndrome. These pathways apparently do not pass via the first thoracic ganglion into the lower portion of the stellate ganglion, as previously reported by others in the literature and in various texts.

Massive Prolapse of the Rectum

The Pemberton-Stabins Operation for the Cure of Procidentia

MORTON J. TENDLER, M.D., Memphis

Prolapse of the rectum is defined as a pathological protrusion of one or more layers of the rectal wall through the anus. Extrusion of the rectal mucous membrane alone is termed prolapse of the mucous membrane, as seen in children and in the aged. Extrusion of all the layers of the rectal wall is termed prolapse of the rectum, or procidentia. Aggravation and prolongation of the procidentia may lead to further extrusion of the lower bowel involving the rectosigmoid and sometimes the sigmoid. The further weakening of the peritoneum of the cul-de-sac of Douglas and the transversalis fascia leads to the inclusion of loops of ileum in the hernial sac. In massive prolapse one may find involved not only rectum, but also rectosigmoid, sigmoid colon, and ileum.

The subject of this paper concerns the report of a case of massive prolapse of the rectum operated upon by a combination of two procedures. The Pemberton operation was first reported in the *Transactions of the Southern Surgical Association*, in 1938.[5] The Stabins procedure was reported in *Surgery* in 1951.[9] The patient, a white male 41-year-old engineer, was admitted to the Baptist Memorial Hospital on Sept. 10, 1953, operated upon Sept. 14, and discharged two weeks later. He was rechecked from time to time, and at his last examination, in March, 1955, eighteen months after surgery, there was no recurrence. Bowel movements occur twice daily, normally.

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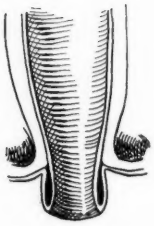
ETIOLOGY OF MASSIVE PROLAPSE

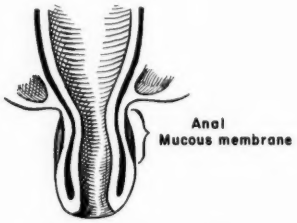
Interest of surgical anatomists has been centered upon the cause of massive prolapse for many years. The pioneer studies and dissections of Zuckerkandl,[10] Moschcowitz,[4] Graham,[2] and others have led them to believe that massive prolapse is a true hernia through the pelvic transversalis fascia. The transversalis fascia is, as a rule, strong enough to retain all the viscera in the peritoneal cavity, except at certain points, namely, where blood vessels or viscera make their normal exit. It is at these points only that hernia occurs. Any abnormal increase in intra-abdominal pressure, incident to straining, trauma, parturition, or protracted coughing or vomiting may initiate hernia. Prolapse may also occur in ascites, constipation, diarrhea, urethral obstruction, advancing age, malnutrition, wasting disease, and often in the insane.[1] As described by Moschcowitz, prolapse develops when the contents of the cul-de-sac (rectosigmoid, small bowel, sigmoid) push the apex of weakened cul-de-sac and the anterior wall of the rectum into the ampulla or lumen of the rectum. The lateral walls of the rectum fold inward and follow through the sphincter, to appear externally as a gradually enlarging mass. This mass, as it enlarges, contains not only rectum but also a peritoneal sac filled with large and small intestine. The anal sphincter is usually continent, playing rarely any part in the pathological picture.

Figures 1, 2, and 3 represent the outline forms of prolapse of the rectal mucous membrane, prolapse of the rectal wall, everting the anal canal, and true procidentia with a retaining anal canal and sulcus.



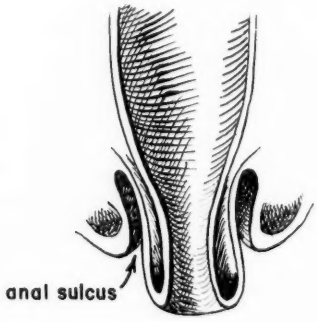
PROLAPSE OF RECTAL MUCOUS MEMBRANE

Fig. 1.—A protrusion of the mucous membrane alone. Not an uncommon occurrence in infants and in old age. Often accompanies hemorrhoids.



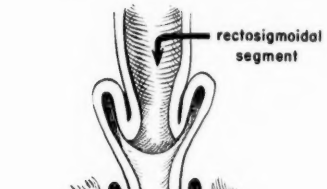
SIMPLE PROLAPSE OF THE RECTUM

Fig. 2.—This degree of prolapse involves all layers of the rectal wall, everting the anal mucous membrane. There is no anal sulcus within the external sphincter muscle, retaining the anal canal.



PROLAPSE OF THE RECTUM
(true procidentia)

Fig. 3.—True procidentia. The anal canal and sphincters act like the intussuscipiens in an intussusception, with a retaining anal canal and anal sulcus.

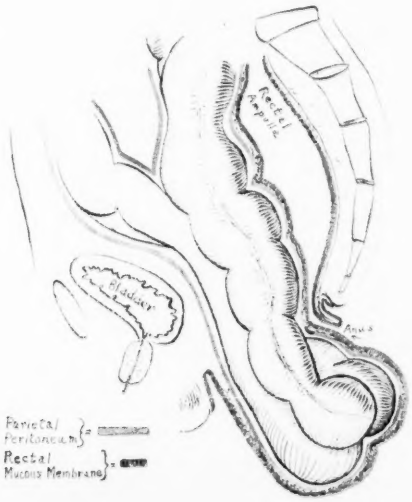


PROCIDENTIA PLUS RECTOSIGMOIDAL INVOLVEMENT
(intussusception of rectosigmoid)

Fig. 4.—Early massive prolapse. Rectosigmoidal segment (or intussusceptum) should be pictured as invaginating the anterior ampullary or rectal wall, though in some cases a true intussusception may occur.

Figure 4 outlines the early form of procidentia with rectosigmoidal involvement. The upper segment (the intussusceptum) should be pictured as invaginating via the anterior ampullary or rectal wall. In Figure 5 (sketched after the manner of Roscoe Graham) is a cross section of a massive prolapse as it appeared in the patient to be presented in this report. Fortunately, these prolapses

Fig. 5.—Sketch, after Graham, revealing extent of procidentia in patient presented. Small bowel, as well as redundant sigmoid, fill the hernial sac.



TYPE OF PROCEDURE	CASES	RECURRENCES	
		NO.	PERCENTAGE
PEMBERTON	56	5	11.4
MOSCHCOWITZ	55	29	63.0
OTHER INTRA-ABDOMINAL	15	4	33.3
PERINEAL PROCEDURES	62	27	57.4
TOTALS	188	65	43.6

Fig. 6.—From Pemberton, Kiernan, and Pemberton: Annals of Surgery, **137**:478, 1953, J. B. Lippincott Company. An imposing array of cases from the Mayo Clinic, showing the excellent results obtained in the Pemberton procedure alone. See Pemberton and Stalker.[5]

are rare. Their repair (aside from the great controversies in establishing their pathological anatomy) has been the subject of innumerable papers, with a great variety of operative procedures. Most reports contain one or at most a few cases. It is difficult to arrive at conclusions as to the efficacy of most of the procedures because of the paucity of cases and results reported.

In reviewing the voluminous literature on the subject of massive prolapse, Simon and Williamson, in 1946,[7] detailed a summary of 19 separate and distinct types of procedures employed. Many of these were reported enthusiastically by well-known surgeons. There are three groups of procedures: perineal, intra-abdominal, and combinations of perineal and intra-abdominal operations.

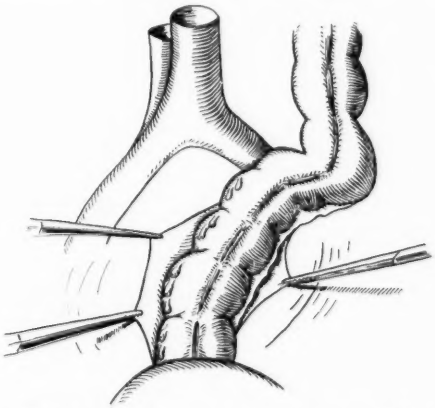


Fig. 7.—The first stage of the Pemberton-Stabins operation. Exposure of the extraperitoneal tube of the rectum, its ampulla, and lower rectosigmoid, down to the anal sphincters—with complete mobilization of all segments (Pemberton procedure).

The first clear picture came into focus when Pemberton, Kiernan, and Pemberton[6] reported the experiences of the surgeons at the Mayo Clinic, in 1953. They summarized a total of 188 cases operated upon during the past 40 years. There were 121 intra-abdominal and 62 perineal procedures in the series. The recurrence rate in the perineal operations was 57.4%. In the Moschcowitz-type procedure 63.0% failure was recorded. In a catch-all group of intra-abdominal procedures the recurrence rate was 33.3%. Their best results, in 44 cases done by the Pemberton technique, followed two years or longer, were but 11.4% (Fig. 6).

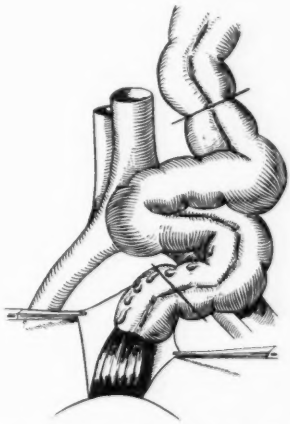


Fig. 8.—The second stage of the Pemberton-Stabins operation. Resection of the redundant, heavy sigmoid and proximal segment of the rectosigmoid.

The principle of the suspension-fixation operation of Pemberton was developed by John de J. Pemberton[5] after he noted the fixation of the rectum in an elevated position in operations of exteriorization for lesions in the rectosigmoid and upper rectal segments. Complete mobilization of the rectum from the hollow of the sacrum resulted in the formation of stout scar tissue in the retrorectal space, thus securing the rectum in its elevated position. He proceeded to mobilize the rectum down to the tip of the coccyx, elevating also the pelvic colon, thereby straightening out the rectosigmoid and rectum. Holding the rectum taut, the perito-

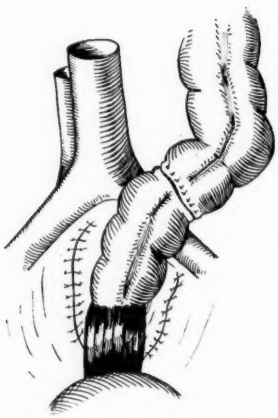


Fig. 9.—The third stage of the Pemberton-Stabins operation. End-to-end anastomosis between the iliac portion of the colon and the distal segment of the rectosigmoid. The "tautness" of Pemberton is here emphasized, in pulling up the extraperitoneal rectal segment.

neum and transversalis fascia were closed high, obliterating the cul-de-sac. Interrupted sutures were used to fixe the upper bowel to pelvic and abdominal walls, and to the uterus in the female.

A series of such unfortunate cases, with only 11% recurrence, is indeed a remarkable accomplishment. One should consider, however, the intra-abdominal findings in these patients—a greatly thickened visceral peritoneum (Zuckerguss type, as in perisplenitis), which greatly increases the weight of the long, prolapsed rectosigmoid and sigmoid and often adhesions between the loops. The redundancy has been retracted manually from the outside world and deposited upon a not-too-strong pelvic fascia. The few fixation sutures may hold, or they may soon loosen. The Pemberton recurrences may be due to this pathological phenomenon, with the heavy weight of the thickened peritoneum constantly bearing down upon the delicately sutured transversalis fascia and peritoneum. Skinner and Duncan [8] noted this puzzling picture, and they proposed and performed a colostomy to fix the redundant bowel high in the left iliac quadrant. Hulten,[3] in 1946, besides obliterating the cul-de-sac (Moschcowitz) resected the redundant sigmoid by the Mikulicz procedure. He did not perform the excellent Pemberton procedure.

In 1951, Stabins reported two cases in which he not only used the Pemberton technique but also resected, with end-to-end anastomosis, the entire redundancy of the rectosigmoid and sigmoid colon. Figures 7, 8, and 9 detail the operation as performed in the following case report, after Stabins.

REPORT OF A CASE

A 41-year-old white male engineer was admitted to the Baptist Memorial Hospital on Sept. 10, 1953.

Chief Complaint.—Dropping of rectum on defecation.

Present Illness.—Onset about 10 years ago, when he noticed he had hemorrhoids and rectal bleeding. Home remedies (liquid petrolatum, warm baths, and rectal ointments) gave him temporary relief. About a year later he became progressively constipated. During the ensuing years, straining, plus the use of strong purgatives, aggravated his hemorrhoids and bleeding. For the past two years more and more of his rectum would be extruded at every stool. Great difficulty was often experienced in attempting reduction. For the past year it has been necessary to assume the knee-chest position in order to accomplish complete reduction. There has been no

Fig. 10.—Straining, in the lithotomy position, the procidentia measures 8 in. from perineum to the apex and 6 in. in diameter at its greatest circumference.

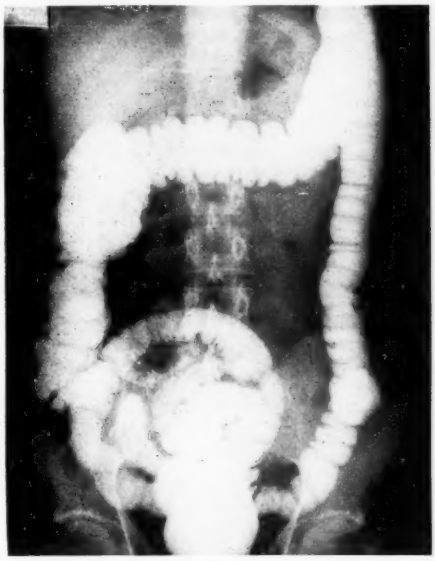


Fig. 11.—Barium enema reveals a doubled redundant sigmoid and rectosigmoid, with no other abnormalities.

incontinence or protrusions between defecations, no recent loss of weight, and no formed stools, since purgation is now necessary to obtain a copious bowel movement every other day.

Past History.—No major illness or surgery.

Marital History.—Married. Father of two normal children.

Fig. 12.—Photograph taken 15 months after surgery. Rectal (digital) examination reveals normal sphincteric tone. Excessive straining, during which time photograph was taken, produces no protrusion. There is no protrusion in any position upon straining.

Review of Systems.—Except for nervousness and fits of depression, due to his rectal condition, there were no significant factors. His appetite was good, his urinary function, normal, and his sexual history, normal.

Physical Examination.—Weight 139½ lbs.; height 5 ft., 6½ in.; temperature 99 F; pulse 84; respiration 16, and blood pressure 150/90.

The patient was a slight, erect white male of early middle age, not apparently ill. He was intelligent and cooperative. Examinations of the head, neck, heart, lungs, and abdomen revealed no abnormal or pathological findings. Extremities and genitalia revealed no disease or abnormalities.

Fig. 13.—Barium enema (15 months after surgery) reveals a normal rectocolonic formation, with easy barium evacuation.

The Local Lesion (Fig. 10).—With the patient in the lithotomy position, straining revealed marked procidentia. It measured 8 in. in length and 6 in. in diameter at its greatest circumference, measured in the squatting position, as at stool.

In the knee-chest position reduction was accomplished without great difficulty. The anal sphincter was in normal tone. The prostate gland was small.

Laboratory Findings.—Blood and urine examinations were within normal limits; Kahn test was negative.

Proctoscopic and Sigmoidoscopic Examinations.—A thickened, edematous, superficially ulcerated rectal, and sigmoidal mucosa.

Barium Enema.—No filling defects, polyps, diverticula, or gross ulcerations. Excepting for a

redundant sigmoid and rectosigmoid, there were no abnormalities (Fig. 11).

Bowel Preparation.—Two ounces of castor oil was given on the day of admission.

Low Residue Diet.—Phthalylsulfathiazole (Sulfathalidine), 2 gm. q 4 h for 48 hours, and vitamin K, 25 mg. four times a day. Neomycin (Mycifradin) 1000 mg. was started 48 hours before surgery and given every four hours and the phthalylsulfathiazole discontinued. A gastroduodenal tube was inserted before surgery. The patient was operated upon Sept. 14, 1953.

Operation.—

Anesthesia: Intravenous thiopental (Pentothal), intratracheal cyclopropane, curare.

Incision: Left paramedian, suprapubic.

Position: Extreme Trendelenburg.

Exploration revealed the marked sigmoidal and rectosigmoidal redundancy with its greatly thickened and whitened walls. Marked evidence of a chronic, friction-type of peritonitis, as seen in old herniae, was demonstrated. This traumatic type of peritonitis involved mainly the pelvic and cul-de-sac peritoneum, the rectosigmoid, the entire sigmoidal loop, and parts of the terminal ileum (Fig. 5).

The Pemberton-Stabins operation was then performed (Figs. 7, 8, and 9). The resected colon measured 18 in. in length.

The end-to-end anastomosis united the ampulla of the rectum and the descending colon at the level of the iliac crest, by the double row method of McNealy.

A cecostomy, with a large de Pezzer catheter inserted into the anterolateral wall of the caput cecum, was done before closing the abdomen. A large de Pezzer catheter was secured in the lower rectum, reaching just above the anal canal. These two "safety valve" de Pezzer catheters are routine with the operator in segmental resections.

Two units of blood were given during surgery. The time of operation was two and one-half hours. The immediate postoperative blood pressure was 130/70; pulse rate, 88.

The Trendelenburg position (3-in. elevation of foot of bed) was maintained for 10 days. The gastrodoudenal tube was removed on the second postoperative day. Liquid stools appeared through the rectal tube on the fourth day. The cecostomy tube was removed on the fifth day.

The patient was discharged on his 15th postoperative day. His incision was well healed. One-half pint enemata of isotonic saline (250 cc.) were given twice a day during his last week in the hospital. Upon discharge he was advised to continue half-pint saline enemata twice daily and to avoid all straining efforts.

The patient reported six weeks after surgery, Oct. 29, 1953, that he had gained 5 lbs. since discharge. He reported two bowel movements daily, one following his enema in the morning and another, spontaneously, without straining, at night. Rectal examination reveals normal tone. Excessive straining produces no protrusion in any position (Fig. 12).

Barium enema on Dec. 18, 1953, 15 months after surgery, revealed a normal rectocolonic formation, with easy barium evacuation (Fig. 13).

The patient was last seen on Aug. 15, 1955. His bowels move twice daily without enema or laxative. There has been no protrusion since surgery.

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Persistent Invagination of Meckel's Diverticulum

A Cause of Chronic Intestinal Obstruction

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Intestinal obstruction due to Meckel's diverticulum is generally portrayed as an illness of acute onset, often with rapid crippling of intestinal function.* It is evident, however, that in some instances this disorder follows a more deviate pattern, that intestinal obstruction due to Meckel's diverticulum may pursue a subtle recurrent chronic course.†

Meckel's diverticulum, present in 2% of persons, remains silent clinically in the wide majority of cases. This vestigial accessory of the intestine is generally perceived as an innocuous structure, a superfluous congenital anomaly. Its claim to significance usually consists of a remark in an autopsy protocol noting it as an incidental finding at necropsy. The concept that Meckel's diverticulum is a mere anatomical curiosity, although deeply rooted in medical thinking, is not entirely valid. It has become increasingly apparent that the importance of this intestinal anomaly has been underestimated. In recent decades more and more attention has been focused on Meckel's diverticulum because of the frequent and unheralded incidence of pathologic conditions associated with this structure. Owen and Finney [7] in appraising diseases of Meckel's diverticulum found that 25 to 35% of Meckel's diverticula show significant pathologic changes. Among its protean manifestations of disease, Meckel's diverticulum, mimicing acute appendicitis, may be the seat of acute inflammation, Meckel's diverticulitis. The diverticulum, harboring gastric mucosa, may be the site of a bleeding peptic ulcer, the source of serious intestinal hemorrhage.

Intestinal obstruction due to Meckel's diverticulum occurs with greater frequency than is generally realized. Despite the textbook notations that this complication is relatively rare, clinical data indicate that Meckel's diverticulum is, in fact, a relatively common cause of primary enteric obstruction. In statistical studies of intestinal obstruction clinically, Meckel's diverticulum proved to be the underlying cause of obstruction in 2.6% of cases in some series [2] and up to 6% in other studies.‡ In adults intestinal obstruction is the most frequent complication produced by Meckel's diverticulum.[3]

Meckel's diverticulum represents an anomalous persistence of the embryonic yolk-stalk structure. In embryos of three to five weeks, as the abdominal wall closes the foregut and the hindgut form proximally and distally to the yolk stalk. Normally the yolk stalk, also known as the vitelline duct, becomes obliterated after the fifth week. In rare instances the duct persists as a fistulous tract between the intestine and the umbilicus, or the duct may become occluded, leaving the stalk as a narrow fibrotic band between the intestine and umbilicus. Often the portion of the vitelline duct attached to the umbilicus is eliminated, leaving patent a segment adjoining and communicating with the intestine; this persisting portion of the duct extending outward from the ileum forms a tubular blind pouch, the common Meckel's diverticulum.

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* References 1, 2, and 3.

† References 4, 5, and 6.

‡ References 8 and 9.

Meckel's diverticulum and related remnants of the yolk stalk may bring about intestinal obstruction in a variety of ways. In some instances the diverticulum or a fibrotic remnant of the yolk stalk extending across the peritoneal cavity may entwine loops of intestines and provoke volvulus and strangulation.

Invagination of Meckel's diverticulum into the ileum is one of the most important mechanisms by which the structure produces intestinal obstruction. The inverted diverticulum, projecting as a polypoid mass in the lumen of the ileum, may offer serious interference to the flow of intestinal contents. Ischemic and inflammatory changes are prone to occur in the inverted and distorted diverticulum. Of great hazard, the invaginated diverticulum may provoke an intussusception of the intestine in the segment adjoining the diverticulum. This condition is not rare. Harkins,[1] reviewing the literature in 1933, found 160 cases of inversion of Meckel's diverticulum with enteric intussusception. The incidence of Meckel's diverticulum in males is three to four times greater than in females; reflecting this high incidence in males, inversion of Meckel's diverticulum is a disorder predominantly affecting males; in the series reviewed by Harkins,[1] 79% of cases of inverted Meckel's diverticulum occurred in males.

Clinically, in most cases there are abdominal pain, vomiting, distention, and other signs of acute intestinal obstruction; most patients with acute symptoms are treated surgically. The invaginated diverticulum, together with the intussuscepted intestine usually present at operation, is in most instances readily reducible; however, removal of a portion of the intestine with the diverticulum is usually necessary because of local ischemic changes.

Not all cases of inverted Meckel's diverticulum are acute. Although this condition is usually thought of as a rapidly evolving surgical emergency, there are an important number of cases which do not follow this acute pattern. A large Meckel's diverticulum may become invaginated and occupy the lumen of the ileum without precipitating clinical symptoms. Heller § reported an instance in which an inverted Meckel's diverticulum, hanging freely in the lumen of the ileum, was encountered at autopsy; no related symptoms had been apparent in the patient during life.

In addition to the acute group and the asymptomatic type of case, a third clinical pattern, pertinent to the present study, may evolve: Invagination of the diverticulum may develop and persist for long periods and clinically be associated with a recurrent or chronic form of intestinal obstruction. Lower [5] and others have emphasized that in patients with inverted Meckel's diverticulum the clinical course often suggests chronicity. Harkins,[1] Bennecke,[9] Hertzler and Gibson,[4] and other observers have described cases of invaginated Meckel's diverticulum in which the clinical course of the patient was long and punctuated by recurrent or chronic symptoms of intestinal obstruction. Of the 41 cases reviewed by Hertzler and Gibson, 9 patients suffered many or repeated attacks of intestinal obstruction; in one case monthly episodes recurred over a period of five years; in one symptoms were present continuously for six months. Typically in this type of case symptoms of obstruction, though persistent, are only of moderate severity; despite careful study clinically, the cause of the obstruction remains an enigma. Ultimately, such cases may culminate in an acute attack of obstruction, requiring surgical intervention. At operation in chronic cases of this type, the inverted Meckel's diverticulum presents as a finger-like projection in the lumen of the ileum; peritoneal adhesions within the hollow of the inverted diverticulum tend to prevent reduction and withdrawal of the saccular structure from the lumen of the intestine by the surgeon.

In considering the syndrome of chronic intestinal obstruction due to persistent inversion of Meckel's diverticulum, the final diagnosis must be based on a correlation of clinical and pathological findings. In identifying this process it is requisite that the chronic nature of this intestinal disturbance

§ Heller, cited by Kuttner.[10]

not only must be evident clinically but also must be proved pathologically. Considerable difficulty may be encountered in appraising the duration of the invagination of Meckel's diverticulum. Although the clinical course may reflect chronicity, the relative time of onset of the invagination often cannot be clearly established because of equivocal pathological changes in the surgical specimen. In most cases of this nature, even after careful gross and microscopic study of the specimen, the age of the lesion remains open to question.

A convincing example of long-standing invagination of Meckel's diverticulum, a case in which the chronic nature of the process could be clearly confirmed by pathologic study, has heretofore not been readily available. The observation of such a case forms the basis of the present report; in this patient the clinical pattern of chronic intestinal obstruction proved, on pathologic study of the surgical specimen, to be due to an inverted Meckel's diverticulum which presented itself as a fixed lipomatous polyp in the lumen of the ileum.

REPORT OF A CASE

The patient, a 35-year-old white man, presented symptoms of partial intestinal obstruction over a period of two months. In the first three weeks of illness the patient complained of lower abdominal pain, nausea, vomiting, constipation, and weakness. The pain was colicky in nature, unrelated to meals, usually lasted a few hours, but sometimes extended through the entire day. No radiation of pain was present. There was no diarrhea, bloody stools, or melena.

Examination of the patient three weeks after the onset of symptoms revealed his temperature to be 100 F; his abdomen was soft; some tenderness was elicited over the left lower quadrant; no abdominal masses were palpable. There was a well-healed appendectomy scar. The physical examination otherwise revealed no significant abnormalities. White-blood-cell count was 7900. Urinalysis revealed no significant abnormalities. The stool was guaiac-positive. Slight fever continued during the fourth and fifth weeks of illness. Lower abdominal pain and vomiting continued. In the sixth week, white-blood-cell counts of 20,300 and 14,700 were recorded. During the following weeks, symptoms of obstruction tended to increase. X-ray studies, repeated during this period, showed evidence of small-bowel obstruction.

Throughout the clinical course, the patient's condition fluctuated widely; some days he was free of complaints; at other times there was moderate abdominal discomfort. At no point was the patient's condition considered acute or critical.

Two months after the onset of symptoms, because of the recurring symptoms of intestinal obstruction and because of the roentgenographic evidence of intestinal obstruction, an exploratory laparotomy was performed. An obstruction was found within the ileum approximately 18 cm. from the ileocecal junction; an intraluminal mass was palpable within the involved segment of intestine. A segmental resection and end-to-end anastamosis was performed. The patient subsequently made a rapid recovery.

Lumen of ileum; inverted Meckel's diverticulum presenting as a lipomatous polyp of the small intestine; the inverted diverticulum, sectioned longitudinally, shows a compact central core of adipose tissue.

The specimen examined in the surgical pathology laboratory was a segment of ileum 40 cm. long. At one point on the serosal surface, on the antimesenteric aspect of the intestine, there was an irregular funnel-shaped indentation, approximately 20 mm. wide, directed obliquely inward toward the lumen of the intestine; a smooth lobulated pad of adipose tissue about 3 cm. wide was present at the margin of the indentation; a portion of this fat pad was tucked into the hiatus and tightly anchored

there. The intestine distal to the obstruction, considerably dilated, measured 5 to 6 cm. in diameter; the proximal segment was 3 to 4 cm. The external conformity of the intestine was otherwise undisturbed; there was no intussusception of this segment of the ileum. Palpable within the lumen of the resected intestine was a sausage-like mass approximately 12 cm. long.

When the segment of intestine was laid open, a reddened, finger-like, polypoid mass 12 cm. long and 2 cm. wide was revealed (Figure); the polyp was attached to the lining of the intestine at a point corresponding to the indentation on the external aspect of the intestinal segment; the free end of the polyp was directed distally. The elongated mass, firmly rooted at its base, filled the lumen of the intestine snugly. Grossly, the mucosa of the intestine appeared to be continuous upward and around the polyp. When the polyp was incised, a sharply delineated outer layer of dense tissue approximately 3 mm. thick covered the mass; at the base of the polyp this coat was continuous with the circumjacent intestinal wall. The central portion of the polypoid mass was packed firmly with adipose tissue, pale and turgid (Figure).

It was readily evident that the polypoid mass in the distal ileum was a Meckel's diverticulum inverted into the lumen of the intestine. The hollow of the inverted structure, with the peritoneal margins effaced, had become occupied by adipose tissue. The central column of adipose tissue provided a broad core for the polypoid structure. Anatomically, a long Meckel's diverticulum is usually provided with an independent mesentery; it is evident that, with the inversion of the diverticulum, the mesenteric fat had been drawn into the peritoneal hollow and there incarcerated.

Histologic examination revealed that the thick outer coat of the polypoid structure consisted of mucosa and muscularis which was continuous with that of the adjoining ileum. A thick zone of chronic inflammation with hyperplastic small blood vessels lay deep to the muscularis; beyond this, toward the broad central core of the polypoid structure, there extended a uniform accumulation of adipose tissue. The wall of the inverted diverticulum, particularly the mucosa, showed moderate to severe inflammatory alteration; destructive changes were severest in the mucosa about the tip of the polypoid structure.

COMMENT

The mechanism which brings about inversion of a Meckel's diverticulum is a matter of question. It is evident that a long and wide diverticulum is more likely to become inverted than a short diverticulum of narrow caliber. The phenomenon of inversion is apparently the result of excessive peristaltic action built-up in the wall of the diverticulum; in an effort to expel its luminal contents, the diverticulum, its tip unanchored, literally turns itself "inside-out." In some instances the diverticulum, poised as a long polypoid structure in the ileum, tends to remain inverted. In the present case adipose tissue derived from the mesentery of the diverticulum filled the peritoneal hollow of the diverticulum. The peritoneal surfaces within the diverticulum, subjected to a chronic inflammatory reaction, became effaced. In the course of time the incarcerated adipose tissue became tightly adherent; the diverticulum was rendered irreducible. The invaginated diverticulum was in this manner converted to a lipomatous polyp.

Inflammatory changes in the polyp structure were probably of ischemic nature. It is likely that in the course of time the blood supply, critically disturbed in the invaginated and distorted diverticulum, proved inadequate; infarctional changes associated with inflammation followed. The process of local inflammation together with the mechanical obstruction produced by the inverted diverticulum ultimately provoked the clinical pattern of chronic intestinal obstruction evident in this case.

The clinical and pathological manifestation of chronicity can be closely correlated in this case. Clinically, the duration of the process extended over a period of two months; however, grossly and microscopically the pathologic changes evident in this specimen indicate that the invagination of the diverticulum was likely of greater age.

SUMMARY

The importance of Meckel's diverticulum increases as its role in provoking intestinal obstruction becomes more widely recognized. In recent decades it has become apparent that Meckel's diverticulum is not merely an innocuous congenital anomaly; it is, in fact, the cause of a variety of serious intestinal disorders.

Intestinal obstruction due to Meckel's diverticulum, occurring most commonly in adults, is generally depicted as an acute surgical disease. This concept is not entirely adequate. It has been suggested in the past that Meckel's diverticulum may be responsible for a form of intestinal obstruction of chronic nature; however, definite confirmation of such a process, chronic in nature, by pathologic studies has heretofore not been available.

In the present case, a young adult, observed over a period of two months, showed recurring episodes of incomplete intestinal obstruction. At operation a mass was found in the ileum; on pathologic investigation the obstructing mass proved to be an inverted Meckel's diverticulum, which in the course of time had evolved as a lipomatous polyp of the ileum.

The pathologic findings in this case demonstrate that an inverted Meckel's diverticulum may give rise to chronic intestinal obstruction. Although uncommon, this etiologic factor merits due clinical consideration in patients, particularly males, who have protracted or recurrent symptoms of intestinal obstruction.

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Unusual and Complicated Lesions of the Biliary Tract and Their Treatment

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INTRODUCTION

My colleagues and I feel greatly honored that one of us has been asked to present the Eighth Walter Estell Lee Lecture. Dr. Lee was known intimately and admired by members of our surgical staff who preceded me. I, too, was fortunate in having a chance to become acquainted with him during the latter part of his surgical career. He was indeed a worthy Philadelphian, for he was born here, educated here, and spent all of his life in this community.

In his memoir of Dr. Lee, Dr. Jonathan E. Rhoades stated: "As is often the case with men of multiple activities, it is difficult to single out a particular achievement representing the culmination of a long career. It is sufficient to say that Walter Lee rose purely on his own merits, to be Chief of Staff of the oldest hospital in the United States, Chief of Surgery in the oldest children's hospital in America, Head of the Department of Surgery in the first graduate school of medicine in America, Chairman of the Editorial Board of the oldest surgical journal in America, and an officer of sixteen years of America's oldest surgical association of national scope."

Although I referred to Dr. Lee as a Philadelphian, born, educated, and carrying on his work here, it seems to me that he typifies the adage about "the lengthening shadow of man," especially of the men who occupied important surgical positions in this and the other fine medical schools in Philadelphia. I am thinking particularly of such men as Samuel Gross, J. William White, W. W. Keen, Frazier, Deaver, Muller, and many others. The activities and surgical work of these great clinical surgeons and teachers continue to influence even the present generation. It may interest some of you that Dr. J. William White presented funds for a traveling scholarship to the Mayo Foundation, which enables one of our graduate fellows to visit foreign surgical clinics every two years.

For my part, I have been visiting clinics in Philadelphia since 1924, and these visits have been a source of scientific profit and personal satisfaction. My final 14 months of active duty in the Navy during World War II was in your fine U. S. Naval Hospital. During these war years, many Philadelphia physicians and surgeons were on its staff. The civilian surgeons of this city and members of the Philadelphia Academy of Surgery were always willing to and did contribute in every way possible to better the treatment of the patients and to advance the program of surgical training which we older officers on the staff were carrying out for the younger men.

I have mentioned these things because it has been through the teachings of the men whom I referred to and the man whose memory we are honoring this evening that Philadelphia has always been one of the centers most active in advancing clinical and investi-

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gative surgery. I think that I could add to Dr. Rhoades' summary of Dr. Lee's career with the comment of one of his pupils and admirers, who said, "Dr. Lee felt that better men were on the way in surgery and he wanted to have a part in making them better."

Dr. Lee's scientific contributions number more than 90 and associated with him as co-authors were men distinguished then and later for their own work. Dr. Lee's contributions cover practically the entire field of surgery. He was particularly interested in thoracic diseases, and his contributions on the delayed closed treatment for empyema during World War I reduced the mortality from a high of 40% for early open operation to 4% for a delayed closed one. This was one of his earliest great contributions, and his revisions and co-authorship of the Stewart and Lee surgical text is another.

I regret that time does not permit any elaboration concerning his surgical contributions or his philosophies and character beyond this too brief comment.

LESIONS OF THE BILIARY TRACT

One of the most fascinating fields for study is that involving lesions of the biliary tract. Some of the reasons for this are that a lesion in the biliary tract is hardly ever entirely localized, since portions of the tract are present within the liver and the lower portion of the common bile duct is surrounded by the head of the pancreas in two out of three cases. It is apparent that inflammation in the wall of the gall bladder or the bile ducts is likely to extend through them to the structures in which they begin, course, and end and that obstructive lesions in any of them directly affect the others. Disturbances of the biliary tract, broadly speaking, are due to infection and obstruction; each can produce the other. In many instances they occur together and cause pain and frequently jaundice. It is under these two main topics, pain and jaundice, that I wish to develop my presentation of unusual lesions of the biliary tract, for the usual ones are well known.

SOME CAUSES OF PAIN IN BILIARY DISEASE

When a patient has attacks of pain in the right upper quadrant that are frequently associated with qualitative food dyspepsia, and when such a patient is found to have a diseased gall bladder with or without stones on cholecystographic examination, the removal of the gall bladder usually, but not always, relieves the symptoms. But what were the causes of the pain and dyspepsia, and, if these symptoms should persist after cholecystectomy, what is to be done about them? I have no intention of discussing the neurologic aspects of pain caused by lesions of the biliary tract other than to say that within the biliary tract pain is caused by intermittent obstruction and distention of the gall bladder or the bile ducts, usually associated with inflammation and frequently with infection. With this in mind it is well to pause and refer to a few of the causes of increased pressure within the common bile duct, their clinical and roentgenologic demonstration, and the relation of increased pressure to pain.

Increased Intraductal Pressure.—Several years ago, McGowan, Butsch, and I,[1] studying the pressures within the common bile duct of patients following choledochostomy, were able to reproduce attacks of severe pain in the right upper quadrant (biliary colics) by increasing this pressure, either by the rapid introduction of fluid into the duct or by the production of spasm at the lower end of the common duct by administration of morphine, codeine, and other substances. A radiopaque fluid used for the injection enabled us not only to study ductal pressures but also to observe the effects of these procedures on the biliary tree—that is, on the size, the obstruction, the spasms, and the emptying time—and to note and record the effects on the patients. When antispasmodics, such as glyceryl trinitrate (nitroglycerin) and amyl nitrite, were given, spasm of the sphincter of Oddi and the adjacent duodenum subsided, the duct emptied, the ductal pressure decreased, and the patient's pain subsided. These studies explained one aspect

of the causes of biliary colic. The important question then to be determined was the effect of cutting the sphincter of Oddi, since duodenal spasm was noted with the sphincteric spasm.

In 1952, I described * two cases in which I had performed sphincterotomy for postcholecystectomy biliary colic. A short T-tube not extending through the cut sphincter was left in the common duct for drainage in each case, and it also was used for postoperative choledochography. Narrowing of the pancreatic portion of the common bile duct was visualized, and the common bile duct above this was dilated. At that time, I indicated that it would be well to study intraductal pressures and visualize the extrahepatic bile ducts following sphincterotomy. The use of a short T-tube instead of a large one would permit the study of intraductal pressure and roentgenologic studies of the biliary tree in a sufficient number of cases for one to evaluate the operation. The main purpose of a long T-tube extending through the divided sphincter and left in for several weeks rather than a short T-tube seems to be the prevention of fibrous contracture at the site of the sphincterotomy. However, if the incision through the sphincter is made accurately and extended sufficiently to open the ampulla, contracture should not occur, provided that the cut wall of the duodenum and the wall of the duct are approximated by suturing, as has been my custom. Only an incision of such accuracy and length can lay open the interior of the ampulla sufficiently so that the main opening of the pancreatic duct can be seen and the duct catheterized to determine whether obstruction is present.

In a case of stricture of the common duct which had been repaired over a short T-tube, I was able after removal of the T-tube to introduce a straight catheter into the duct and wash out through the fistulous tract some stony material which had accumulated in and above the ampulla of Vater. Therefore, I reasoned that a straight catheter could be introduced into the common duct through the fistulous tract after the removal of a long T-tube also, and this would permit the same physiologic studies with regard to intraductal pressure, obstructions, and ductal emptying as a short T-tube. By this procedure, whether fibrous contracture had or had not occurred at the site of the sphincterotomy could be ascertained.

Studies were carried out in two recent cases by my assistants, Scimeca and Harris, and me. In one a long T-tube had been used, which extended through the divided sphincter of Oddi; when it was removed, it was replaced by a catheter in the common duct. In the other patient a short T-tube was used after sphincterotomy. A radiopaque thorium substance, thorium dioxide (Umbrathor), was injected into the common duct through the short T-tube nine weeks after sphincterotomy in this case. The intraductal pressure increased almost immediately, and the patient complained of the same severe epigastric pain that she had had previous to sphincterotomy. Thorium dioxide was used because the patient was allergic to iodine preparations. That a radiopaque substance injected into the common duct through a T-tube to obtain a choledochogram would produce pain in the absence of obstruction was not anticipated, but when it did occur, its significance was recognized. The pain was partially relieved by glyceryl trinitrate. A delayed roentgenogram made some minutes later showed retention of the radiopaque dye within the bile ducts. Yet, duodenal contents were readily aspirated from the T-tube an hour later.

On repeating the study the following day, we found that with the attacks of pain intraductal pressure increased to more than 300 mm. of water, and spasm of the lower end of the duct with reflux into the pancreatic duct was visualized roentgenologically. It seemed worth while to study the effects of splanchnic block with procaine in this case because of its successful use in some previous cases in which, at operation, no cause was found within the biliary tract, the liver, the

* Walters, W., in discussion on Lyday.[2]

pancreas, or the duodenum to explain the patient's pain. Consequently, needles were inserted into the left and right splanchnic regions, and procaine hydrochloride was injected to block the left splanchnic nerve. The location of the needles was confirmed roentgenographically. Within three seconds, the pain was relieved. X-ray examination at this time still showed spasm of the lower end of the duct, with retention of the radiopaque media in the common duct and in the pancreatic duct. The intraductal pressure was still high and static at about 250 mm. of water. A second injection of thorium dioxide was given then to increase intraductal pressure. The epigastric pain did not return, but the patient had a feeling of fullness to the right of the incision. The right splanchnic nerve was not blocked with procaine at this time.

In the other case the long T-tube was removed, and a catheter was introduced into the common duct 13 weeks after sphincterotomy. The usual radiopaque iodine preparation for choledochography, sodium iodomethamate (Neo-Iopax) was injected through the catheter a little more rapidly than normally. The shadow of the common duct was noted fluoroscopically, and at the same time the intraductal pressure was studied. With the increased rapidity of injection, distention of the biliary tree took place, spasm was noted in the lower part of the duct, the intraductal pressure increased, and the epigastric pain returned. Glyceryl trinitrate relieved the pain and decreased the intraductal pressure. The following day the study was repeated. This time thorium dioxide was used instead of sodium iodomethamate. Results were similar to those observed in the other case, except that reflux of the material into the pancreatic duct could not be demonstrated.

The first patient returned to the Mayo Clinic nine weeks later for further observation. She had been free of pain and had gained in weight. The second patient continued to have mild attacks of pain at intervals but obtains relief by the sublingual administration of nitroglycerin.†

Spasm of Common Bile Duct Indicated as a Cause of Postcholecystectomy Pain by Results of Sphincterotomy or Choledochoduodenostomy or Both.—These studies and others have led me to review a group of cases in which I had performed sphincterotomy or choledochoduodenostomy or both for the relief of postcholecystectomy pain when no cause ‡ for the pain, except dysfunction of the sphincter of Oddi or pancreatitis, was found within the biliary tract or adjacent structures. In the sphincterotomy group two of the nine patients followed five months or more had complete relief of symptoms, and four were improved, with less frequent and less severe pain or only occasional episodes (Table). These patients seemingly were satisfied with their operation. Of those undergoing choledochoduodenostomy, two obtained complete relief of their pain, three were partially relieved, and three seemed little benefited. In the small group having the combined procedures either in one or two stages, none had excellent results and three continued to have pain.§

It seems evident, with an appreciable percentage of patients continuing to have attacks of pain after sphincterotomy or choledochoduodenostomy or both, that ductal spasm or some cause within the liver, the pancreas, the duodenum, or the nervous system may be present.

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† Prior to sphincterotomy this patient had five months' relief of her attacks of pain by alcohol injection into her left splanchnic nerve done on two separate occasions.

‡ I have seen ulcers on the posterior duodenal wall penetrating into the pancreas, lesions of the right kidney and adrenal gland, regional enteritis, and abdominal carcinomatosis produce painful symptoms suggesting biliary tract disease and thought to be due to biliary dyskinesia or the postcholecystectomy syndrome.

§ I am indebted to one of my former first assistants, Dr. James C. Lowe, for an earlier review of a small group of these patients.

Stone and Stricture.—It seems apparent that spasm of the wall of the common duct as well as of the sphincter of Oddi can cause pain. I should like to describe to you two other cases which are informative. The biliary colics in the first case occurred after cholecystectomy. At operation one stone was found in an anomalous, accessory, large right hepatic duct, and another was floating in the midportion of the common duct, and neither had produced any jaundice. The biliary colics of the second patient resulted from contraction after a duct-to-intestine anastomosis for postcholecystectomy stricture. Operation showed the stoma to be only 2 or 3 mm. in diameter. In this case the lesion had not produced any jaundice.‖ It is natural to expect dilatation of the common duct above a recurring stricture, but that as small an opening could cause pain without jaundice is further evidence of the painful effects of spasm of the common duct.

I have found dilatation of the common duct in all patients with common duct stones on whom I have operated, except, possibly, those with 1-mm. bile-pigment stones, and 33% of the patients with a stone in the common duct have not had jaundice. Many of the stones in the common duct are small, and many of them float in the bile and are not impacted in the ampulla, but some of them are not small and are in the ampulla and still do not cause enough continuous obstruction to produce jaundice. This also indicates that the floating stone in the common duct, as well as the ampullary stone, that produces attacks of pain without jaundice, does so as a result of spasm of the wall of the bile duct with which there may be associated spasm of the sphincter of Oddi.

Contribution of Studies with Sodium Iodipamide (Cholografin) to Differential Diagnosis: My colleagues in the departments of roentgenology and gastroenterology and I have found that iodipamide studies of the common duct have been helpful in certain cases in which one is attempting to incriminate lesions of the biliary tract as a cause of the so-called postcholecystectomy syndrome. Stones 1 cm. in size or larger which are present within the bile ducts are usually well shown, but smaller stones frequently are not. An additional value to this laboratory procedure is to visualize the size, conformation, continuity, and emptying time of the bile ducts and in this respect to give evidence of incomplete obstruction of the duct. There has been, however, a 16% error in the accuracy of the method as a diagnostic procedure per se, and even with good concentration of the dye the bile ducts may fail

Results of Sphincterotomy, Choledochoduodenostomy, or Both for Biliary Dyskinesia

Operation	Total	Recent Operation †	Result *			
			No Improvement ‡	Attacks Less Severe	Fair to Good	Excellent
Sphincterotomy and choledochoduodenostomy						
At same time	5	1	3	..	1	..
Choledochoduodenostomy first	2	1	1	..	..	..
Sphincterotomy	15	6	3	3	1	2
Choledochoduodenostomy	9	1	3	..	3	2
Total	31	9	10	3	5	4

* Follow-up after last operation, whether choledochoduodenostomy, sphincterotomy, or both, from 5 months to 2 years 5 months.
† Recent operations or no follow-up.
‡ No improvement or later operation.

‖ I have just operated on another such patient in whom the choledochoduodenal anastomosis had contracted down so that its opening could not be demonstrated at operation. Her biliary colics were frequent and severe, without fever or jaundice, and they were relieved completely for two weeks by injection of alcohol into her left splanchnic nerve.

to show sphincteric or ductal spasm or small calculi, even though tomographic studies are made also.¶

The Pancreatitis Associated with Obstruction of Pancreatic Duct.—Obstruction of the pancreatic duct will produce pancreatitis and pain and other severe symptoms which are usually accompanied by elevations in the level of the serum amylase. At operation brawny induration with edema is noted in and around the pancreas, and occasionally there is adjacent fat necrosis. Recently I removed by multiple incisions in the head of the pancreas six calcium carbonate stones (8 to 10 mm. in diameter) from dilated branches of pancreatic ducts of a patient who was having frequent severe and disabling attacks of pancreatic pain. Sphincterotomy was done, but the opening of the pancreatic duct could not be identified. I was able to pass a small ureteral catheter through one of these dilated branches into the opening of the main pancreatic duct in the ampulla, which I had been unable to identify because of an overlying flap of duct wall. A ureteral catheter was then passed through the opening in the pancreatic duct in the ampulla into the main pancreatic duct. The site of the duct and catheter was demonstrated roentgenographically. One end of this catheter was left in the pancreatic duct for drainage and the other was brought out of the abdomen through the duodenum. A long T-tube was used to drain the common duct, the distal portion of which was passed through the divided sphincter of Oddi into the duodenum. This relieved the patient's painful seizures, and the T-tube and the catheter were removed later by the home physician. The patient replied to a questionnaire four months after operation by saying that the attacks of severe epigastric pain which he was having daily prior to his operation had completely subsided.

¶ In the recent case referred to in the previous footnote, although the duct was somewhat enlarged, the Cholografin study did not show the extreme degree of contraction of the choledochoduodenostomy stoma.

My colleagues, Berens, Baggenstoss, and Gray,[3] in a study of the pancreas obtained at necropsy in 16 cases of pancreatitis, found that the main pancreatic duct (Wirsung) was greatly dilated in the tail of the pancreas in seven cases, and they observed histologic evidence of dilatation in the smaller ducts and ductules in four other cases. Factors contributing to dilatation of the main duct were pancreatic lithiasis in two cases, choledocholithiasis in two cases, and foci of necrosis and inflammation in three cases. They advised surgical treatment of retrograde decompression of the pancreatic duct by amputation of the tail of the pancreas and pancreaticojejunostomy. Gray and, later, others have carried out this procedure, and in one reported case a chronic pancreatic fistula which had persisted after prolonged drainage of a pancreatic cyst closed rapidly and completely.

The frequent association of recurring pancreatitis with disease of the biliary tract is well known, and relief of pain when these two lesions are associated is frequently striking after removal of a diseased gall bladder, usually with prolonged drainage of the common bile duct. The causal relationship of reflux of bile into the pancreatic duct to pancreatitis is somewhat confused by the recent demonstration by Kleitsch [4] that in 10% of cases the main pancreatic duct empties into the duodenum through a separate ampulla caudad to the ampulla of Vater, and in an additional 60% a large accessory branch drains the main pancreatic duct through a separate opening in the duodenum. This makes a total of 70% of cases in which an increase of pressure in the common bile duct, with reflux of bile into the pancreatic duct, would not increase pressure in the pancreatic duct. Moreover, recently, Parry, Hallenbeck, and Grindlay,[5] using a new method of measuring intraductal pressure without obstructing the duct in dogs, have shown that pressures within the pancreatic duct exceed those within the common bile duct. Further confusing the pressure mechanisms in the ampulla of Vater is the fact that in some of the

cases in which I have done sphincterotomy, and have searched for the ampullary opening of the pancreatic duct, a flap of mucous membrane has been lying over it. In such cases with an intact sphincter of Oddi, an increase in pressure in the biliary duct would tend to close the ampullary opening into the pancreatic duct by pressing the flap over it.

These anatomic variations may explain why some patients with obstruction of the common duct have associated pancreatitis and others do not. The important fact remains, however, that one patient, having attacks of biliary colic subsequent to sphincterotomy, had an increase of pressure in the common bile duct as a result of spasm of the common bile duct and in another patient reflux of a radiopaque substance into the pancreatic duct could be seen. This patient received immediate relief of pain from injection of the left splanchnic nerve with procaine. The other patient had obtained the same result for a long period after two previous alcohol blocks of the left splanchnic nerve. That the relief of pain is not due alone to relief of intraductal pressure is evidenced by the increased intraductal pressure found in the demonstration of the retention of the radiopaque material within the common duct. The corollary of this, it seems to me, is that sphincterotomy is a valuable procedure and may be followed by excellent results in some cases in which spasm or inflammation of the sphincter of Oddi is producing intermittent attacks of biliary obstruction with increased biliary pressure, especially if reflux of bile into the pancreatic duct results. However, a continuation of the attacks may be expected if spasm of the common duct occurs after sphincterotomy. On the other hand, in those cases in which the common bile duct is dilated and the head of the pancreas is swollen, the possibility that sphincterotomy will not relieve the pain and that choledochoduodenostomy will, must be entertained. I have had successful results following choledochoduodenostomy in several such cases, whereas in some others both procedures were necessary, either simultaneously or on different occasions to give relief of the attacks of pain—not always, I am sorry to say, complete relief of symptoms.

OBSTRUCTIVE JAUNDICE

I have elaborated on causes of pain in relation to the lesions of the biliary tract and the pancreas in cases without sufficient biliary obstruction to produce jaundice, for the presence of obstructive jaundice is an immediate indication for the location of the obstructing lesion. When a patient has jaundice associated with pain in the right upper quadrant of the abdomen, the problem at operation is to exclude the presence of stones within the common or hepatic ducts of the ampulla of Vater by opening the common duct, by carefully exploring the interior of the common and hepatic ducts with scoops, by irrigation of the duct, and by passing scoops or probes through the ampulla into the duodenum and carefully palpating the duct over the scoop, for sometimes scoops slip past a stone in the ampulla or duct. Operative cholangiography may be used to supplement but not to replace this type of accurate exploration of the duct. In the absence of stones in the duct and at the ampulla, the surgeon must be careful to exclude a small malignant lesion in or around the ampulla, and it may be necessary to open the duodenum to do so. Landry and I [6] have reported some cases in which very small lesions of the ampulla of Vater or the papilla of Vater were responsible for the patients' attacks of biliary colic and jaundice and could only be identified by opening the duodenum. In most cases of obstructive jaundice there is little difficulty in making a correct diagnosis at operation and in carrying out the proper surgical procedure, if a careful exploration of the bile ducts and ampulla is carried out.

Recently, I saw a patient on whom I did a radical resection of the Whipple type # for a Grade 3 carcinoma of the ampulla of Vater,

The operation consisted of resection of the head of the pancreas, the duodenum, the lower end of the stomach, and the lower portion of the common bile duct.

in 1946. At that time it was thought that suturing over the cut end of the pancreas and the pancreatic duct was a satisfactory method of handling the cut portion of the pancreas, and this was done in his case. Three years later because of attacks of abdominal pain which were thought to be due to recurrence, abdominal exploration was carried out. No recurrence was evident nor were there metastatic implants. The distal half of the pancreas was shortened and rounded like a piece of rope. The patient has continued to have attacks of epigastric pain requiring morphine for relief about two or three times a year. His general health, however, has remained excellent, and he is working just as before he had his operation. I recently examined him and found him to be in excellent condition, except for some hemorrhoids for which he had an operation.

Tumors of the Head of the Pancreas.—Finding an enlarged head of the pancreas at operation, when there are no stones in the gall bladder or common duct and no other causes for the obstructive jaundice, raises the question of whether radical resection of the head of the pancreas and its adjacent structures or a more conservative biliary intestinal anastomosis should be carried out. Punch biopsy of the pancreas with the Silvermann needle has been valuable if a positive microscopic diagnosis of carcinoma can be made. Failure to make this diagnosis, however, does not exclude the possibility of carcinoma. I believe that it is unsafe to cut too deeply into the head of the pancreas to obtain a specimen and prefer to rely on palpatory evidence, which to date has been extremely satisfactory.

Whenever the surgeon is in doubt concerning the nature of the tumor or whether it can be removed completely, the best procedure, in my opinion, is cholecystenterostomy or choledochoduodenostomy followed by another exploration in four to six weeks. I have seen a few striking examples in which the tumor completely disappeared after this procedure and the patient remained well for several years. One such patient, on whom I performed a cholecystogastrostomy in 1933, is still alive and well. His pancreatic tumor may have been a syphilitic gumma.

The results of radical resection of the lower end of the common duct, the head of the pancreas, and the duodenum for lesions of the papilla of Vater have always been worth while. The five-year survival rate of such patients at the Clinic, as recently reported by Giberson and Waugh,* has been 38%. Similar radical procedures have been used for malignant lesions of the head of the pancreas and have been followed by few survivals beyond 18 months. In recent years, however, when my colleagues and I have limited our radical resections for lesions of the pancreas to those patients with small carcinomas of the head of the pancreas, the five-year survival rate has increased to 15.8%. The advantage and the value of these procedures in cases of localized ampullary carcinomas and in cases of small carcinomatous tumors of the head of the pancreas are obvious. The operative risk at the Clinic for these lesions, as determined by Giberson and Waugh, was one death in 24 cases (4.2%).

When the malignant tumor extends into the neck and body of the pancreas, the recognition of this extension to the remaining portion of the pancreas must be determined immediately by frozen-section examination of the cut end of the pancreas. If malignant cells are found in this location, the remaider of the pancreas must be removed. This is not a difficult procedure if the spleen is used as a handle for elevating the tail and body of the pancreas, ligating the splenic artery and vein close to their origin. One patient who underwent this procedure has just returned to his home in excellent condition.

Intrahepatic Pericholangitis.—Intrahepatic pericholangitis, described by Watson, Hoffbauer, and Howard,[7] produces pain frequently associated with jaundice without any evidence of obstruction in the extrahepatic

* Giberson, R. G., and Waugh, J. M., unpublished data.

biliary tree. I have seen and operated on several such patients, the diagnosis being based on biopsy of the liver and the absence of extrahepatic biliary obstruction confirmed by postoperative cholangiography. The clinical picture as well as laboratory data in these cases indicated biliary obstruction but did not localize it to the liver. Indeed I have seen an occasional patient with cirrhosis of the liver whose attacks of pain, associated with jaundice, simulated those of extrahepatic biliary obstruction. These patients with intrahepatic pericholangitic biliary obstruction have been relieved of the jaundice by prolonged T-tube drainage of the common duct. Itching frequently is a serious and disabling symptom of biliary cirrhosis. Strangely enough with T-tube drainage of the common duct it tends to subside and sometimes disappears almost completely, only to recur after removal of the tube and to subside again after its reinsertion at a later date. The mechanism for this is not well understood but may be related to the fact that the sphincter of Oddi adds some extrahepatic obstruction.

POSTOPERATIVE STRICTURES OF THE BILE DUCTS

Before closing, I should like to consider briefly my experience in the treatment of postoperative stricture of the common duct over the past 31 years in 380 cases.[8] Such patients are seriously ill not only as a result of the biliary obstruction and the associated biliary and intrahepatic infection but also because of the effects of the bilirubinemia on all the organs and tissues of the body. Times does not permit an elaboration of the problems involved in the management of these patients if the surgical risk is to be only 4% to 6%, other than to say that cooperative management with the internist and the clinical physiologist is of the utmost importance. Recognition of the disturbances of liver function, proper preoperative preparation, and the proper use of vitamin K, fluids, electrolytes, and blood before, at, and after operation have contributed to the safe performance of surgical procedures which relieve the biliary obstruction, even though most of the patients in my series had previously had two or more unsuccessful operations.

In these cases, when once it is recognized that injury of the common duct has occurred, relief of the obstruction should be done as early as possible, for delay means recurring obstruction and infection, hepatic dysfunction, and, finally, hepatic decompensation and death. Practically the only patients with stricture of the common duct who cannot be benefited by surgical procedures in which relief of the obstruction is obtained are those patients who have hepatic decompensation. It is a matter of personal preference whether a surgeon uses the biliary-duodenal or biliary-intestinal anastomosis with an enteroanastomosis, or a Roux-Y anastomosis in the jejunum. I have preferred, whenever possible, to use the biliary-duodenal anastomosis because reflux into the biliary tree after this procedure has not been found either clinically or experimentally to produce cholangitis, because the operation is less complicated, and because bleeding or the effects of fistulous drainage, should they occur, are confined to a small region which in many cases permits an almost extraperitoneal operation.

Cholangitis which develops after biliary-intestinal anastomosis is due to obstruction at the anastomosis, regardless of the type, and I have proved this at operation on patients, with all the different types of anastomosis. It is most astonishing that such an anastomosis can contract down to a few millimeters in diameter and produce only attacks of pain, without jaundice and fever. This is another excellent example of the fact that spasm of the common duct will produce pain.

COMMENT

In closing, I should like to express my appreciation to the pioneers and earlier investigators in this field in which I have reported from my personal experiences at the Mayo Clinic. Mirrizzi, of Argentina, was the first to perform operative cholangiograms. Mallet-Guy, Bergeret, and, recently, Sou-

pault and Caroli, of France, have added materially to knowledge of the abnormal physiology of the common bile duct with studies of pressure in the biliary duct and cholangiographic studies during and subsequent to operation. The studies of Mulholland and Doubilet on division of the sphincter of Oddi; of Whipple, Parsons and Mullins, Brunschwig, Waugh, and Clagett on radical resection of the head of the pancreas for carcinoma; of Lahey, Cattell, and Cole on treatment of strictures of the common bile duct; of Ravdin, Rhoades, Fitzhugh, and their associates on the effect of intraductal pressure on the cardiac mechanism, and of Ravdin on changes in the liver resulting from use of different types of anesthetics are all great contributions. Some of these men began the work in the fields which I have referred to, and others have extended it. Many others, too, deserve great credit for their contributions which have advanced knowledge in this interesting and frequently complicated field of surgery. I am sorry that time does not allow me to elaborate on the significance of their particular contributions.

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Meconium Peritonitis Associated with Fibrocystic Disease of the Pancreas

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Perforation of the intestine during intrauterine, intrapartum, or early neonatal life may result in extravasation of meconium into the peritoneal cavity, causing a severe sterile and usually fatal peritonitis. Most reported cases have been associated with mechanical obstruction, diverticula, intestinal ulceration, and perhaps obstetrical trauma. Numerous cases have been reported in which no explanation for the perforation could be found. In 1943, Agerty and his associates [1] recorded the first report of a case of meconium peritonitis treated surgically with survival of the infant. Since Agerty's report, at least 25 survivals following operation have been added to the literature. Detailed descriptions of the salient pathologic and clinical features of this condition have been presented by Boikan,[2] Agerty,[1] Low and his associates,[3] Olnick and Hatcher,[4] Bendel and Michel,[5] and others.

The following case report is that of an infant with meconium peritonitis operated upon for intestinal obstruction on the fifth day of life. The clinical course and operative findings are unusual only in that the condition occurs infrequently and survival following operation is relatively uncommon. Of added interest in this case, however, is a later proved diagnosis of fibrocystic disease of the pancreas.

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REPORT OF A CASE

A five-day-old white male infant was transferred from an outside obstetrical service to the Roper Hospital on March 12, 1955, because of abdominal distention. At the time of birth of the child, intense bile-staining of the amniotic fluid, vernix, and skin was noted by the obstetrician, and, since the mother was Rh-negative, the possibility of erythroblastosis fetalis was considered. The child appeared to be vigorous and active. He was not jaundiced and his spleen was not palpable. His weight was 3630 gm. A Coombs test on the infant's blood was reported as negative. Routine newborn orders were written, and an evaporated milk formula was started at 12 hours of age. On the fourth postpartum day, it was noted that, although the child had been taking his formula well, his bowel movements were scanty and contained only a small amount of meconium. The child again appeared well to examination. The following day his abdomen became distended, and it was reported that his only stool in the previous 48 hours had consisted of a small amount of slightly greenish mucus. The child had continued to take his formula very well, and he had not vomited since birth. At the time of transfer to Roper Hospital, the infant did not appear ill and was well hydrated. The abdomen was distended and seemed to be tender to palpation. Peristalsis was present but was hypoactive. Physical examination revealed no other unusual findings.

X-rays of the abdomen demonstrated dilated loops of intestine and scattered flecks of calcified material throughout the area of the peritoneal cavity. A barium enema was done which demonstrated a complete obstruction of the colon at the splenic flexure.

Exploration of the abdomen was carried out through a supraumbilical transverse incision. When the peritoneum was incised, a collection of serous fluid was encountered which occupied the entire right upper quadrant and contained irregular particles of green granular material. The fluid was encapsulated by a thick wall of brownish-yellow material which was firmly adherent to liver, stomach, colon, small bowel, and abdominal wall. Loops of small and large bowel were agglutinated

by fibrous and fibrinous adhesions and in many areas were densely adherent to irregular clumps of gritty, brownish-yellow material. Many of the loops of intestine were distended, with intervening segments of bowel completely collapsed. One large deposit of the foreign material was densely adherent to the colon at the splenic flexure and appeared to be producing an obstruction there. By rather tedious dissection separation of the adherent loops of bowel was carried out from the ligament of Treitz to the lower sigmoid area. An effort was made to remove as much of the foreign material as possible. Careful examination of the entire bowel revealed no area of perforation. Small particles of firm material were palpated within the colon, but no evidence of meconium ileus was present. No evidences of obstruction other than those due to inflammatory adhesions were present, and no diverticula were found. The peritoneal cavity was irrigated with Hartmann's solution containing penicillin and streptomycin, and the incision was closed in layers with interrupted 0000 nonabsorbable surgical (silk) sutures. The child received 50 cc. of blood during the procedure. Cultures of the material from the peritoneal cavity were sterile and the microscopic appearance of the material was consistent with meconium.

At the completion of the operation, the child was cold, clammy, and cyanotic, and respirations were of a gasping nature. He was placed in an incubator receiving oxygen and was given an additional 100 cc. of whole blood, after which his condition improved strikingly. Within six hours after operation the child's color and respirations were good and he was crying vigorously. In addition to maintenance intravenous fluids, he was given procaine penicillin G (Crysticillin) 150,000 units and streptomycin 100 mg. intramuscularly every 12 hours and cortisone 12.5 mg. intramuscularly every six hours. The child's course thereafter was surprisingly satisfactory. He began passing dark-green stools on the second postoperative day, and after a short episode of mild abdominal distention on the fourth postoperative day he began to take oral feedings well. On the eighth postoperative day he was taking 3 oz. of formula every four hours and was having five or six normal-appearing stools daily. The dosage of cortisone was gradually reduced and was discontinued on the 11th postoperative day. He was discharged from the hospital 15 days after operation, in excellent condition.

During the first three weeks following discharge from the hospital, the child gained weight steadily, took his formula well, and continued to have normal bowel movements. However, it was noted that he had a persistent cough, and moist rales were heard over the lung fields repeatedly. On April 8, 1955, clear alkaline duodenal aspirations, both before and after methacholine (Mecholyl), were obtained and were found to have no trypsic activity. A test for lipase activity was done by feeding the infant iodized oil (Lipiodol) and testing his urine for iodine. No iodine was present in a 24-hour collection of urine.

The child is being maintained on pancreatic extract with the addition of vitamins to his formula, but during the last three of his four months since operation he has had a stormy course. He has had frequent respiratory infections and has been admitted to the hospital once because of dehydration due to diarrhea. His prognosis because of the pancreatic fibrosis is extremely poor. He has had no evidence of intestinal obstruction.

COMMENT

Meconium peritonitis associated with fibrocystic disease of the pancreas, in the absence of demonstrable meconium ileus, has been reported infrequently. Nash and Smith[6] recorded one such case, in which the characteristic changes in the pancreas were found at autopsy. These authors suggested that a temporary obstruction to the bowel may occur on the basis of meconium ileus, with relief of the obstruction at the time of perforation by passage of meconium into the peritoneal cavity. A similar sequence of events has been discussed in regard to unexplained intestinal perforations by Landsteiner,* Kornblith and Otani,[7] Low and his co-authors,[3] and Maguire and Moore. In 1952, Franklin and Hosford reported two cases of meconium peritonitis surviving operation, one of which was later shown to have complete absence of pancreatic enzymes in samples of duodenal contents.

Although the combination of pathologic processes presented here has been seldom reported, a high percentage of the case reports of children surviving operations for meconium peritonitis describe symptoms of slow weight gain after recovery from operation, intermittent diarrhea or constipation, and recurrent respiratory infections. These reports strongly suggest the probability that some of the children have unrecognized pancreatic deficiency. The presence of fibrocystic disease of the pancreas in a child who has survived an operation for meconium peri-

* Landsteiner, K., cited by Low and co-workers.[3]

tonitis requires a guarded prognosis for long-term survival. Examinations of stools and duodenal contents in all cases in which no definite obstruction can be demonstrated should establish a diagnosis of pancreatic deficiency, if present, and should add to our understanding of the pathogenesis of many of the cases of unexplained intestinal perforation with meconium peritonitis.

SUMMARY

A case of meconium peritonitis associated with fibrocystic disease of the pancreas is presented. It is suggested that this association may occur more frequently than has been recorded in the literature and that the association should be suspected and looked for in every case of meconium peritonitis without a clear explanation for perforation.

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The Perineoabdominal Operation for Cancer of the Rectum

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The combined abdominoperineal operation of Miles concededly embodies the best surgical principles known today for the eradication of cancer of the rectum. However, its many disadvantages, such as frequent difficulties in technique, hemorrhage, prolonged operative time, etc., leave much to be desired when one compares it with the more perfected state of many other operations. The second or perineal stage can usually be accomplished quickly and with little difficulty, since the terminal rectum is superficial in the perineum. However, in the abdominal stage the surgeon may be confronted with serious problems when attempting to remove the upper rectum, since not only is this portion of the gastrointestinal tract inaccessible normally but the presence of adherent inflammatory tumors only adds to the problems.

PURPOSE

The purpose of this report is to present the advantages of first performing the perineal stage of the combined operation of Miles, thus reversing the order of operating as originally promulgated by him about 50 years ago. In 1907, impressed by Wertheim's work on cancer of the uterus, Miles abandoned the single perineal operation for cancer of the rectum and suggested the combined abdominoperineal approach.[6] This work of Miles represents the greatest single contribution to the surgical treatment of cancer of the rectum.

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At the present time, one of the successful methods to overcome the difficulties of operating in the depths of the pelvis and to shorten the operating time is the plan of using two surgical teams working simultaneously in the perineum and inside the abdomen. Lloyd-Davies first described this operative plan in 1939, as performed at St. Mark's Hospital in London.[5] However, this method does not seem to be the complete solution to the problem, since few operating rooms today are in so fortunate a condition as to possess that many skilled surgeons, nurses, and lay help. Besides, the presence of so many persons around a single operating table can often lead to a state of confusion. We have found that we can simplify the operation just as well by commencing the operation at the perineum and then later completing the procedure in the abdomen.

INDICATIONS

No patient is subjected to this procedure if there is the least possibility that an anterior resection can be satisfactorily done and a permanent colostomy avoided. Preoperatively, x-rays are carefully studied and digital and sigmoidoscopic examinations are made to evaluate properly the level of the tumor from the anal margin. Experience has shown us the failures of anterior rectal resections, especially when an anastomosis cannot be made in continuity with at least 2 in. of uninvolved rectal wall on either side of the tumor, and with a covering layer of peritoneum over the suture line. But, if the tumor can be felt upon rectal digital examination, or can be seen within the first 5 or 6 in. from the anus with the aid of a sigmoidoscope, then this is considered a suitable

level for a perineoabdominal operation. In doubtful cases, the abdomen may first be opened for an exploration. If there is no opportunity for performing an anterior resection, the abdomen is temporarily closed with several through-and-through abdominal wall sutures of heavy black silk and the perineal stage started first, later completing the work in the abdomen. One would not choose the perineal approach if the case were obviously too advanced for complete excision and the likelihood remained of performing only a palliative colostomy.

If an unavoidable error were to be made and the tumor found to be nonresectable, either during the perineal or, later, in the abdominal stage, the operation could be terminated by reattaching the already partially mobilized rectum to the perineum and fashioning a palliative abdominal colostomy. Fortunately, this complication was not encountered in any of the 17 cases which form the basis for this study. However, from an understanding of the Bacon and Babcock rectal operation and a knowledge of the vascular supply of the rectal wall, such a procedure seems feasible. In the perineoabdominal operation the perineal dissection separates the vascular mesentery of the rectum, together with the perirectal fat and connective tissues along with the rectum, as this structure is loosened from the hollow of the sacrum. In this manner the termination of the inferior mesenteric artery and vein, which are the main source of vascularization to the rectal wall, remains intact. The vessels that may have been severed in the perineum during the freeing of the rectum do not particularly supply the rectum itself. They are the middle and inferior hemorrhoidal vessels, which only supply the rectal wall secondarily by means of anastomoses with the inferior mesenteric artery.[3] Their detachment from the rectum during the mobilization should be of no major consequence, as far as causing rectal necrosis is concerned.

FACTORS INVOLVED IN A COMPARISON OF BOTH OPERATIONS

1. *The Pelvis.*—This anatomical structure contributes to the operating difficulties when one begins the classical Miles operation by entering the abdomen first to free the rectum. Here in the pelvis one is working within a deep, funnel-shaped, immobile structure which makes exposure, illumination, and the manipulation of instruments very difficult. Unlike operations elsewhere in the abdomen, the type of incision used for operating in such depth as the pelvis makes little difference, as far as surgical exposure is concerned, since the most important work takes place at a level far below the abdominal wall opening. Also, varying the type of retractors often is of little help in improving the exposure, since these are placed and retained in position with great difficulty because of the nonresisting bony walls.

In the Miles operation peritonealization in the pelvis is occasionally difficult for several reasons. First, a rectum with walls well infiltrated with fat or with a large tumor may not fit into this limited pelvic space after it is sectioned. This frequently necessitates a wide peritoneal mobilization to cover fully the pelvic contents, a procedure often attended by bleeding and a resulting increase in the extravasation of blood into the pelvis. On the other hand, in the perineoabdominal operation, since the rectum is immediately removed from the pelvis, peritonealization is simplified because the pelvis is empty. One also observes that after the dissection of the rectum has been almost completed in the perineal stage there is a great loosening of peritoneum from the lateral pelvic walls as well as around the bladder. This loosening also facilitates the closure of pelvic peritoneum. The appearance of this loose pelvic peritoneum resembles somewhat the redundant peritoneum observed in patients with long-standing rectal prolapse when one attempts to perform a rectopexy from inside the abdomen (Mikulicz procedure).

2. *Fixation of Rectum.*—As one views the pelvis and its contents from within the ab-

domen, one readily sees that the deepest point in the female pelvis is the cul-de-sac, or the angle where the peritoneum is reflected from the posterior aspect of the uterus and vagina to the anterior wall of the rectum. In the male the analogous lowermost pelvic region is the meeting point of the anterior rectal wall and the posterior surface of the bladder. Thus normally an acute angle is formed between the anterior rectal wall and the uterus and vagina in the female and the bladder in the male. Unfortunately, these areas which can be extremely inaccessible are the principal places where the dissection must be started in order to free the extraperitoneal rectum from its fixed attachments deep in the pelvis.

This acute angulation and low position of the cul-de-sac is due to the normal relationships and fixation of the rectum in the pelvis. For proper bowel functioning, the rectum is maintained in a relatively taut, fixed position, whereby it is anchored distally by the anus to the integument and the soft tissues of the perineum. Proximally, it is fixed by the mesorectum to the anterior surfaces of the lumbosacral vertebrae. In addition, the rectum is in intimate relation throughout its extraperitoneal course with muscular, fascial, and urogenital structures which also contribute to its immobilization. In the male, the most important attachments are the urethra, prostate, seminal vesicles, and bladder, whereas in the female the posterior vaginal wall is in close proximity. In both sexes the encircling fibers of the sphincter ani and levator ani muscles embrace the rectum so as to compress the lumen at different levels. Higher up, near the peritoneal reflection, are the lateral ligaments, or so-called stalks of the rectum, strong fibrous structures on either side which act as lateral guy ropes to steady the rectum in the mid-pelvic position.

If the perineal stage is performed first and the rectum freed from its attachments all the way up to the lateral ligaments and peritoneal reflection, the operation is practically completed and the abdominal operation now becomes a much simplified procedure. Then, a view of the pelvis from within the abdomen readily reveals to the operator that no longer are the pelvic structures inaccessible and at a low level in the pelvis but that the pelvic floor is pushed upward and all organs are within easy reach. For example, the urinary bladder, even though completely emptied of urine, is displaced upward so that it may appear to be a bladder fully distended with urine. Where formerly an acute angle was made by the rectum with the uterus or bladder there is now either an obtuse angle or no angle at all. All fossae and spaces around the rectum, bladder, and other pelvic organs have been obliterated so that a flattened pelvic floor results, but at a higher level. The bladder and rectum are pushed so far upward into the abdomen by the mobilization of the rectum that oftentimes this mass may be seen bulging through the abdominal wall while one is draping the patient for the abdominal incision. The bulge is more pronounced if a good-sized tumor is attached to the rectum. Since the peritoneum is the only remaining layer of tissue separating the freed lower rectum from the abdominal cavity above, all that remains to be done in the abdominal stage of the perineoabdominal operation is to incise the peritoneum on either side of the rectum and to join the incisions in front. The usual difficulty encountered in severing the peritoneum in front of the rectum does not exist any longer. Now it will be evident that the only structures preventing the lifting of the whole rectum and anus from the depths of the pelvis are the rectal stalks on either side of the rectum; but these may be sectioned easily, since they also now occupy a higher and more accessible position.

3. *Adherent Tumors.*—Of course whenever the perineal route is being considered as the first stage in a combined operation one wonders as to whether it would also be feasible to remove tumors of large size as well as those adherent to bladder, uterus, small intestines, etc. However, our experience has been that the technique of separating large adherent inflammatory masses is sim-

pler to perform after the perineal mobilization, bearing in mind that the peritoneal cavity is never entered from the perineal side in the procedure herewith proposed. The early perineal dissection permits such complicating tumors to be pushed upward with the rectum to a level within easy reach of separation from surrounding organs. What previously would have been an attempt to find cleavage planes around fixed organs in the depth of the pelvis now becomes an operation at a much higher pelvic level, with excellent exposure and within easy reach with instruments. Bladder injuries and openings are discovered more readily, since the bladder is projected upward into the operative field. Thus a proper closure and repair of a perforation can be made without any ill after-effect, as the results in several of our patients have shown. In one of our cases a ureter was readily detected adherent to the carcinomatous mass and thereupon easily separated. The general impression prevailed that were the abdominal phase attempted in the beginning as in the operation of Miles the depth and fixation of all structures would never have permitted such a simple ureteral dissection.

There is another maneuver in the abdominal stage to free adherent tumors that utilizes traction upon the distal freed rectum in order to separate a mass that is firmly adherent to surrounding tissues. Whenever a carcinoma of the rectum seems frozen to the bladder or any other pelvic structure, it is advisable to enter the pelvic space quickly by incising the peritoneum around the rectum, pulling up the rectal segment distal to the tumor, and holding taut the rectum on either side of the tumor, endeavoring to dissect the rectal tumor away from any involved structure. We performed this maneuver in two cases just by making traction upon the rubber-covered anorectal region, thereby peeling the rectum away from the bladder. However, it must be emphasized again that the perineal work in the perineoabdominal operation does not extend above the peritoneum, thereby averting serious trauma to any abdominal organs by blind dissection. When a high rectal tumor seems difficult to separate, the operation should be quickly terminated and the abdominal procedure begun. At the second stage it will be much easier to complete the separation of such an adherent tumor from within the abdomen.

4. *Obesity and Acute Intestinal Obstruction.*—The technical difficulties of operating upon obese patients are caused particularly by large overhanging deposits of properitoneal fat in the lateral pelvic walls, which interfere with proper vision and exposure. Therefore, if more dissection can be done in the perineum and less in the abdomen the operating time will be shortened and the procedure simplified. By first mobilizing the rectum from below and permitting it to push upward into the abdominal cavity, the operator will see that very little work remains for the abdominal stage, a distinct advantage when operating upon obese patients.

Secondly, one occasionally encounters a patient with carcinoma of the rectum where, in spite of all efforts at proper preoperative colon preparation, the intestinal loops are still distended with feces and barium at the time of operation. This results in a crowding of the pelvis and abdomen by dilated loops of intestine and the use of many laparotomy pads, often without noticeable effect. In such situations the surgeon can be helped by completing the perineal stage first and entering the abdomen only to incise the peritoneum and the rectal stalks. The resulting use of fewer laparotomy pads and the lessened handling of intestines not only reduce surgical shock but also expedite the end of the operation.

5. *Control of Bleeding.*—A. Hemorrhage from Inferior Mesenteric Vessels: When the Miles operation is performed, it has always been the custom to section these vessels at the outset upon entering the peritoneal cavity. This step can be very difficult at times, especially in an obese patient where the mesentery is heavily infiltrated with fat. Besides, if one is not very familiar with the surgical anatomy of this region, it may be

possible to traumatize a ureter, or even to include it in the ligature.

In the perineoabdominal operation this entire step of preliminary ligation of inferior mesenteric vessels is considered unnecessary, since, as described before, the area supplied by these vessels is the rectal wall itself, a region not involved in the dissection. If the termination of the inferior mesenteric artery (superior hemorrhoidal) is traced into the pelvis after the left colic and sigmoidal branches are given off, the vessel will be seen to diminish rapidly in size and importance as it proceeds along the rectum. It divides into two terminal branches which continue along the rectal wall supplying that viscus. The superior hemorrhoidal artery enters into the blood supply of the perineum only by means of anastomoses with the middle and inferior hemorrhoidal arteries.

Thus one can understand why hemostasis is not dependent upon the preliminary interruption of the inferior mesenteric vessels when mobilization of the rectum is carried out in the beginning. These vessels are sectioned later in the abdominal part of the procedure, after the freed rectum is raised out of the pelvis, the peritonealization has been completed, and the operator is prepared to make the permanent colostomy. At the abdominal stage one can also observe that the mesentery of the rectum is pushed forward and upward with the rectum and other pelvic structures, causing vessels to stand out more prominently for identification. It is then relatively simple to locate the desired point for ligation of the inferior mesenteric vessels, since the whole rectosigmoid with mobilized descending colon can be lifted out of the abdomen in clear view. In this manner what ordinarily would have been a difficult preliminary ligation of the mesenteric vessels in the Miles operation now becomes a minor step in the perineoabdominal procedure.

B. Hemorrhage from Perirectal Tissues: The chief vessels in the tissues surrounding the rectum are the middle sacral artery and the middle and inferior hemorrhoidal vessels. The middle sacral artery, coming down directly from the aorta and traversing the anterior surface of the sacrum, should never bleed, since it is not involved in the dissection. The cleavage plane that separates the rectum with its mesentery from the sacral hollow is anterior to this vessel, and a special effort should be made to preserve it intact. Where one removes the coccyx in order to increase the incision, the middle sacral artery must be secured, since it is cut across. But excision of the coccyx is unnecessary in the perineoabdominal operation as presented here.

The distribution of the middle and inferior hemorrhoidal vessels was described earlier in this report, and mention was made of the presence of the middle hemorrhoidal vessels in the rectal stalks. The middle hemorrhoidals occasionally are of good size, and failure to ligate them may lead to troublesome and serious hemorrhage. The inferior hemorrhoidal vessels are usually not troublesome, but at times they must be clamped on either side before division as they cross the ischiorectal fossae, or, later, after division into smaller branches.[4]

But in spite of the generous use of clamps and ligatures, the perineal rectal dissection may be attended by considerable oozing. This is because of the intimate connective tissue and muscular attachment of the extraperitoneal rectum. Most of the oozing that is not controlled by clamp and ligature results from severed and torn veins on the lateral walls of the pelvis, but this may be suppressed by pressure and packing. From below, the perineal operative wound is difficult to inspect for bleeding, especially since it contains the freed rectum. To locate the bleeding area, one must look upward through the narrow area of rectal dissection.

If clamp and ligature are not successful in controlling the bleeding, the operator would do better to pack the perirectal space tightly with laparotomy pads or gauze, close the skin wound with sutures around the drain, and remove the packs later on through the abdomen at the second stage. There is excellent exposure and visibility in the abdomen after the rectum has been removed,

and any bleeding areas are easily taken care of at this time. If uncontrolled oozing is still present after the laparotomy pads have been removed, then wide gauze packing is placed again into the pelvic space, where it remains after the operation. This packing may be removed gradually through the perineal wound two or three days later.

Another advantage of the perineoabdominal operation is the presence of less blood in the abdominal cavity after the operation is completed. In the Miles procedure blood often leaks upward into the abdominal cavity through the peritonealization suture line, even after the abdomen has been closed and while the patient is being positioned for the perineal stage. However, this cannot happen in the perineoabdominal operation because the peritoneum remains intact throughout the perineal dissection and acts as a wall of protection between the abdomen above and the pelvis below. Besides, all unavoidable blood loss from the extraperitoneal dissection has already been disposed of through the perineal wound. Should there be additional oozing or bleeding, none reaches above the intact peritoneal covering, but it evacuates itself through the perineal drainage tube as the patient's position is being changed for the second stage. A minimum amount of blood remaining in the abdominal cavity thus reduces the possibility of infection.

6. *Asepsis.*—Operations on the colon are more likely to contaminate the peritoneal cavity or the operative wound than any other procedures in the abdomen. All surgeons are aware of the potential dangers of the ever-present aerobic and anaerobic colon organisms. In operations upon the rectum this infectivity of the large intestine is enhanced by several other factors. Devine [3] mentions the septic potentials of the surrounding loose area of the rectum, a space similar to the loose area of the scalp, necessarily capacious because of the great variability in the distention of the rectum.

In the perineoabdominal modification of the combined operation the surgeon can perform a more aseptic procedure than in the operation of Miles. In the first place, before the anus is separated from the skin of the perineum it is closed with a purse-string suture of heavy silk, and, after the incision, a reinforcing layer of sutures approximates the skin edges more closely. Then, after the rectum is completely mobilized and prior to closing the perineal wound, the anus and rectum are covered securely with a rubber glove and pushed upward into the pelvis. Later on, after the abdomen has been opened and the intestines carefully packed away, the pelvic peritoneum is incised and the entire freed rectum is carefully raised out of the pelvis and placed in a Davol rubber bag outside the abdomen without contaminating any part of the surgical field. This maneuver has a great advantage over the steps of the Miles operation, where the rectum is routinely sectioned in the depths of the pelvis. Here the exposed cut ends of the rectum, especially the distal end, must of necessity contaminate the surrounding area as it is buried in the pelvis. However, in the perineoabdominal operation sectioning of the colon takes place outside of the abdomen after the wound is completely closed. Thus the colon is sectioned without the danger of any part of the wound being contaminated. Even though modern methods of colon preparation and antibiotics have helped to diminish postoperative infection, emphasis must still be placed upon the continued adherence to sound surgical principles if we are to continue to lower appreciably the morbidity and mortality of colon carcinoma surgery.

7. *Implantation of Cancer.*—In a recent article by Ackerman and Wheat [1] attention was called to instances of the implantation of cancer in every type of surgical operation including the combined operation for cancer of the rectum. Instances are mentioned where this implantation is an avoidable risk. When cancer of the colon is present, there is usually a discharge of blood, mucus, and exfoliated cancer cells all the way to the anus. In the Miles operation the open ends

of the rectum that have been cut across are potential sources for transplanting cancer cells from the lumen of the colon. Frequently one must section the rectum close to the tumor growth in order to make the rectal mass fit into the pelvis and to be covered over by peritoneum. This affords an opportunity for free tumor cells to transplant themselves somewhere in the pelvic space or in the abdominal cavity. One of our patients developed a recurrence of cancer growth at the colostomy area after a Miles operation, evidently an implantation by instruments or gloves from the original tumor site. With the perineoabdominal technique the anus is immediately closed with sutures, and the large segment of freed rectosigmoid is not sectioned until the abdominal wall is closed, thus eliminating this source of tumor implantation. Besides, the sectioning through the colon takes place after the skin closure at the site for the permanent colostomy, a location at a great distance from the tumor itself.

8. *Operative Shock.*—In operations upon patients for cancer of the rectum, shock may not only occur in the operating room during the procedure but also within the 24-hour postoperative period after the patient has been returned to bed. The principal causes of shock are blood loss, prolonged or excessive anesthesia, operative trauma, and the changing of the patient's position on the operating table.

A. Blood Loss: It is astonishing how rapidly a patient may go into sudden shock from uncontrolled bleeding. While his attention is concentrated upon a difficult dissection, the operator may not be fully aware of the large amount of blood that is sponged out of the operative area. Since extirpation of the extraperitoneal rectum involves the separation of the viscus from closely attached muscular and connective tissue structures, a generous amount of active bleeding and oozing may be present. In the perineoabdominal operation this bleeding takes place in the beginning of the operation, when the rectum is being dissected from below. At this early stage any large or sudden hemorrhage is less harmful to the patient than if it occurred toward the end of the operation in a period wherein the patient may be exhausted from a long and traumatizing operative procedure. In the Miles operation it often has been our experience that as the perineal or second phase of the operation was being completed the anesthetist would inject a warning that the blood pressure was dropping to an unsafe level. This has always been attributed to bleeding and oozing from the perineal tissues that at times can be suppressed only by vigorous packing. However, since performing the perineal dissection first, the anesthetists have been favorably impressed with the better resistance of the patient to blood loss and operative trauma at the beginning of the operation.

B. Anesthesia: Even with the excellent present-day techniques as used by trained anesthesiologists, anesthesia must still be considered as a possible contributing cause of operative shock. One of the advantages in doing the perineal stage at the beginning is the smaller amount of anesthetic necessary to do most of the operative work. If fractional spinal anesthesia is being used, then only 75 mg. of procaine is needed for the perineal stage. Such minimal dosage at a low level in the subdural space is attended by only a slight drop of blood pressure and very little other evidence of spinal shock. If general inhalation anesthesia is being given, only small quantities of the anesthetic gases are required, the patient being carried along principally on thiopental (Pentothal) sodium. Muscle-relaxing drugs, such as curare, are of course not necessary, since the abdomen is not entered in the first or perineal stage.

This minimum anesthesia is then continued until the perineal procedure is completed, the patient positioned, and the abdomen completely draped for the abdominal incision. At this point the level of anesthesia is deepened to provide good surgical relaxation, aided in part by the use of intravenous relaxing drugs. Since the

abdominal part of the operation is easier to accomplish than in the Miles procedure and consumes less time (average 25 minutes) once the perineal stage has been completed, less spinal anesthetic drug and less inhalation anesthetic gas are required. In continuous spinal anesthesia 150 mg. of procaine is sufficient. Such a shortening in the time of deep anesthesia with the sparing use of anesthesia materials is a very welcome improvement to the operation of cancer of the rectum. Here one unfortunately is dealing with older patients, many of whom are the victims of prolonged bleeding, cachexia, and intestinal obstruction, as well as serious cardiovascular and urological disorders.

Our anesthesiologists have repeatedly commented favorably upon the condition of the patients after the perineoabdominal operation, as contrasted with the state of the patients following a Miles resection. At the completion of the modified operation the drop in blood pressure is less, the increase of the pulse rate is not as marked, and the general appearance of the patient is better, when judged in terms of warmth of skin, etc.

C. Operative Trauma: In any combined operation for cancer of the rectum the abdominal part of the operation is usually the more serious stage, as far as operative trauma is concerned. Excessive manipulation within the peritoneal cavity, especially in a field of intestines, will create shock in patients, particularly in the older age group. Occasionally such intraperitoneal trauma is rather extensive because of hindrance to the dissection by large loops of intestine which crowd the operative field. However, in the perineoabdominal operation, since very little work remains to be done in the abdomen to complete the operation, this type of trauma is reduced to a minimum.

D. Position of Patient on Operating Table: We never place a patient on the abdomen for the perineal stage. Many years ago we became aware of the embarrassment to the patient's respiration while lying on the abdomen during anesthesia. We have also observed in many patients after the perineal or second stage of the Miles operation, that, because of the exhausted condition of the patient, the lowering of the legs to the horizontal position from lithotomy was sometimes accompanied by a sharp fall in blood pressure and other signs of shock. The sudden pouring of blood into the lower extremities as they are lowered from the lithotomy position is sometimes enough to deplete the higher centers and the rest of the body of an adequate blood supply. However, since we have been performing the perineal stage first, the ill effects from a shift in blood volume have not occurred, because the patients' condition after the preliminary perineal stage has been good and therefore little affected by the lowering of the legs to the horizontal position. This position is maintained postoperatively while the patient is being transferred to a stretcher and later to his bed.

DESCRIPTION OF PERINEOABDOMINAL OPERATION

1. *Preliminary Preparation.*—The usual preparation for colon-resection patients is used and one has a wide choice of methods. Our patients enter the hospital five to seven days prior to surgery in order to receive proper hydration, bowel cleansing, and treatment with antibiotics. Blood transfusions and electrolyte fluids are given whenever necessary. Bowel cleansing is extremely important and oftentimes will decrease the size of partially obstructed loops. A saline enema is administered daily. A "cocktail" of 2 oz. of magnesium sulfate in 8 oz. of water is given several days before the scheduled operation, provided the bowel obstruction is not so advanced that complete obstruction can be caused. The patient consumes 1 oz. of this purgative mixture every hour for eight doses. The antibiotic used is phthalylsulfathiazole (Sulfathalidine) in 2-gm. doses every four hours. However, if one has only a very short time to prepare the patient, then neomycin is used. If antibiotics must be used by other than the oral route, then streptomycin or injectable chlortetracycline (Aureomycin) and oxytetra-

cycline (Terramycin) are used. A low residue diet is ordered. On the morning of operation a Levin tube is placed in the gastroduodenal region, and a Foley catheter is inserted into the bladder.

2. *Anesthesia.*—This was previously discussed under operative shock. Our choice in selected patients is thiopental sodium and fractional spinal anesthesia, using a polythene catheter in the subdural space.

3. *Position on Table.*—A few additional minutes spent by a member of the surgical team in supervising the positioning of the patient will be well rewarded during the perineal stage of the operation. In the two-team operating technique the position of the patient on the table is obviously more involved in order to provide access to an abdominal wound as well as to a perineal field.[7] However, in the perineoabdominal procedure in one stage only the lithotomy position is required at the outset. At best the perineum is never a comfortable region to operate in for the surgeon and his two assistants.

Our choice of position for the perineal stage is the placing of the patient in the lithotomy position, with thighs flexed on the abdomen and the knees spread apart. The legs are extended somewhat upon the thighs and bandaged in this position to the upright rods of the operating table leg braces; or, to secure a more vertical and higher suspension for the legs, two stands of infusion sets may be used. However, one must always bear in mind the necessity for properly protecting the extremities, not only from skin trauma but also from circulatory obstruction. The flexion of the thighs on the abdomen and the spreading of the knees place the perineal muscles on the stretch so that as they are incised they fall away from the rectum. This position also creates increased size to the pelvic outlet as well as adequate room for the surgeon and assistants to operate.

An additional aid in the exposure of the perineal wound, is the stretching of wide strips of 2-in. adhesive tape from a point 2 in. lateral to the anus to the sides of the operating table. The buttocks are thereby spread well apart, revealing the anal and rectal regions as the dissection progresses. A small hard pillow is placed under the sacrum, thus lifting the buttocks off the table. Since the coccyx is not removed, there is no necessity to raise the sacral region off the table by a sling or other equipment. We prefer to operate while standing, after elevating the table to its maximum height.

4. *Incision.*—Prior to beginning the incision, it is sometimes helpful to stuff the rectum with packing, a useful step when one proceeds with the dissection near the urethra and prostate. Too much packing causes the rectum to crowd the wound and limit the range of maneuvering. The rectum is then closed just within the anal margin by a purse-string suture of heavy black silk. The anus is circumscribed by an incision through skin and subcutaneous tissue a short distance beyond the mucocutaneous junction. Too large an incision is unnecessary, and removal of the coccyx is superfluous.[9] Another running silk suture approximates the edges of the freed skin from side to side, thus further sealing off the rectal opening. The ends of both sutures are left long and serve for traction to move the lower rectum from side to side as the operation proceeds.

5. *Perineal Stage.*—This stage is the most important part of the perineoabdominal procedure. The over-all plan is first to free the rectum down to the levator ani muscles; secondly, to mobilize further the rectum posteriorly and then laterally, and, thirdly, to dissect the rectum anteriorly from the urogenital organs.

Step No. 1. Superficial Perineal Dissection Down to Levator Muscles

The skin incision is further deepened through the subcutaneous tissues and perineal muscles in a circumferential manner at the same time including the sphincter ani muscle. The dissection advances deeper posteriorly and to either side of the rectum, utilizing sharp retractors placed deeply in the wound to facilitate exposure. One seeks

the cleavage plane that separates the perirectal fat from the surrounding tissues. However, in carcinoma of the most distal portion of the rectum one must excise more widely, since growths in this area spread extensively into the ischiorectal space by way of the lymphatics. By means of continued sharp and blunt dissection, the levator ani muscles of the pelvic floor are now exposed, covered by fascia.

Step No. 2. Mobilization of the Rectum Posteriorly and Laterally

A thickened layer of fascia is visible now in the posterior aspect of the wound. This stretches from the front of the sacrum and coccyx to the posterior wall (Waldeyer's Fascia). The next step in freeing the rectum is to penetrate into the presacral space in the hollow of the sacrum. To accomplish this, Waldeyer's fascia must be incised, since dissection posterior to this fascia and too close to the bone will lead to hemorrhage from a plexus of veins going into the sacrum.[8] Also, postoperative urinary retention is apt to persist from interference with the hypogastric plexus. With the operator's left index finger as a guide to locate the tip of the coccyx, this fascia is incised with heavy scissors anterior to the coccyx. This opening is widened to either side with the scissor blades so as to permit the introduction of two to three fingers for dissection posterior to the rectum. Bearing in mind the possibility of traumatizing the middle sacral artery which lies anterior to the sacrum and coccyx, the operator uses the fingers of his left hand to continue to free the rectum posteriorly from the sacral hollow as high up as can be reached. Once a generous space is developed, the dissection proceeds laterally to the levator ani muscles. These are lifted by the fingers away from the rectal wall and sectioned between clamps (Fig. 1). The levators are composed of three main muscle groups: 1. the iliococcygeus, the most superficial group, which is therefore sectioned first, 2. the pubococcygeus, and 3. the puborectalis. The latter two are located more anteriorly and deeper in the pelvis and are sectioned next. In order to delineate properly the attachments of the rectum anteriorly to urethra, vagina, and prostate, a clean and thorough sectioning of all the fibers of the levator ani muscles must be made, thus freeing the rectum from all its muscular attachments to the lateral pelvic walls.

Step No. 3. Mobilization of the Rectum Anteriorly

In the female patient the freeing of the rectum from the posterior vaginal wall is rather easy. But in male patients this separation is much more difficult and involved. In the female patient just a simple dissection by the scalpel is sufficient to complete the anterior mobilization. However, in the male patient the attachments of urethra, prostate, seminal vesicles, and bladder pose a more difficult problem. The Foley catheter may be of help to the surgeon should he stray from the proper plane of dissection. The objective of course is complete freeing of the rectum up to but not through the peritoneal reflection, at the same time saving the sectioning of the rectal stalks for the abdominal operation.

The secret of properly mobilizing the anterior rectal wall in the male patient lies in the ability of the surgeon to locate the fascia of Denonvillier and to continue the dissection through the loose tissue of this space (Fig. 2). This is a narrow area of cellular tissue separating the rectum from the urethra, the posterior surface of the prostate, the seminal vesicles, and the trigone of the bladder. With the fingers of the left hand encircling and grasping the rectum over a piece of gauze, traction is made posteriorly. This helps to place on the stretch the tissues that bind the anterior rectal wall to the urogenital structures under the symphysis. Now it becomes possible to palpate the groove between the prostate and rectum. In order to strike the dissecting space of Denonvillier between rectum and prostate, one must first approach the apex of the prostate and divide a band of muscular fibers, the rectourethralis muscle. This band of fibro-

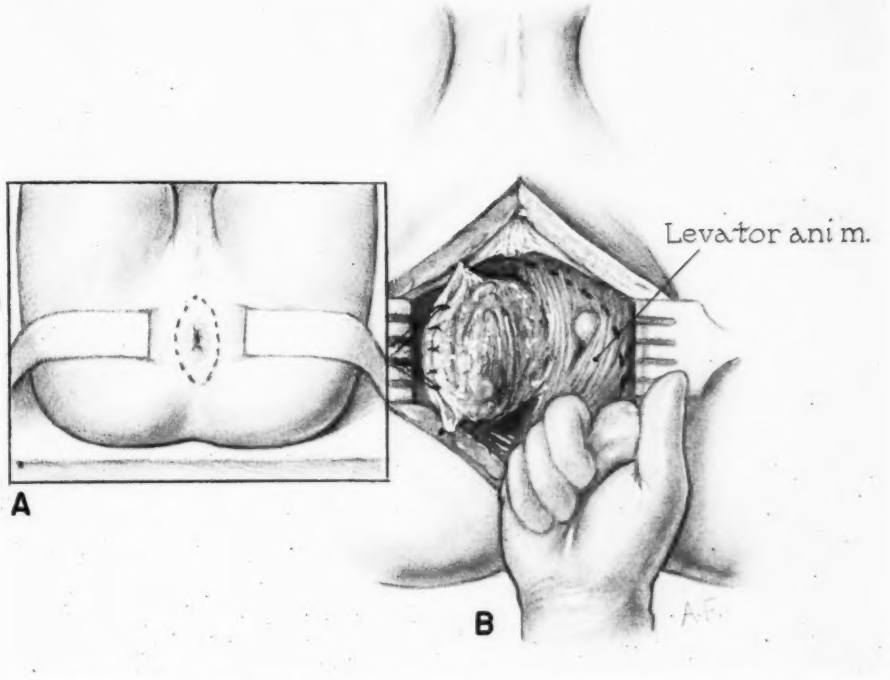


Fig. 1.—Utilization of the fingers to elevate the levator ani muscles to either side of the rectum for sectioning. Insert shows the perineal incision, and the retraction by adhesive strips.

muscular tissue passes from the rectal ampulla to the sphincter urethrae muscle, surrounding the urethra at the apex of the prostate. These diverging fibers should be cut transversely, so that the open blades of dissecting scissors or a hemostat can be introduced between rectum and prostate, thus opening up the space of Denonvillier. The prostate should be repeatedly palpated to make certain that the dissection is in the proper plane. A common source of error is to mistake the prostate for the rectal tumor and to begin the dissection anteriorly to the prostate rather than posteriorly. However, the sudden appearance of perirectal fat between the prostate and rectum immediately assures the surgeon that he is in the proper space between these two structures and that the most difficult step in the operation has been completed. A few more snips with scissor points followed by blunt dissection with finger tips and the prostate is completely freed from the rectum up to the peritoneum. Sectioning of the rectal stalks is not done through the perineal wound, since they lie too deeply in the wound and usually contain good-sized branches of the middle hemorrhoidal arteries, which should be clamped before severance. Without removal of the coccyx, the perineal wound affords inadequate exposure to dissect safely and ligate tissues at such a high level. As will be described later, the rectal stalks or lateral ligaments are easily accessible through the abdominal wound, since mobilization of the rectum has permitted them to rise higher in the pelvis together with the rectum.

In case of more than the usual oozing and if the attempted ligation of bleeding vessels is not successful, then dry laparotomy pads or wide gauze packing may be utilized to stop bleeding. They are pushed into the pelvic space and removed later during the abdom-

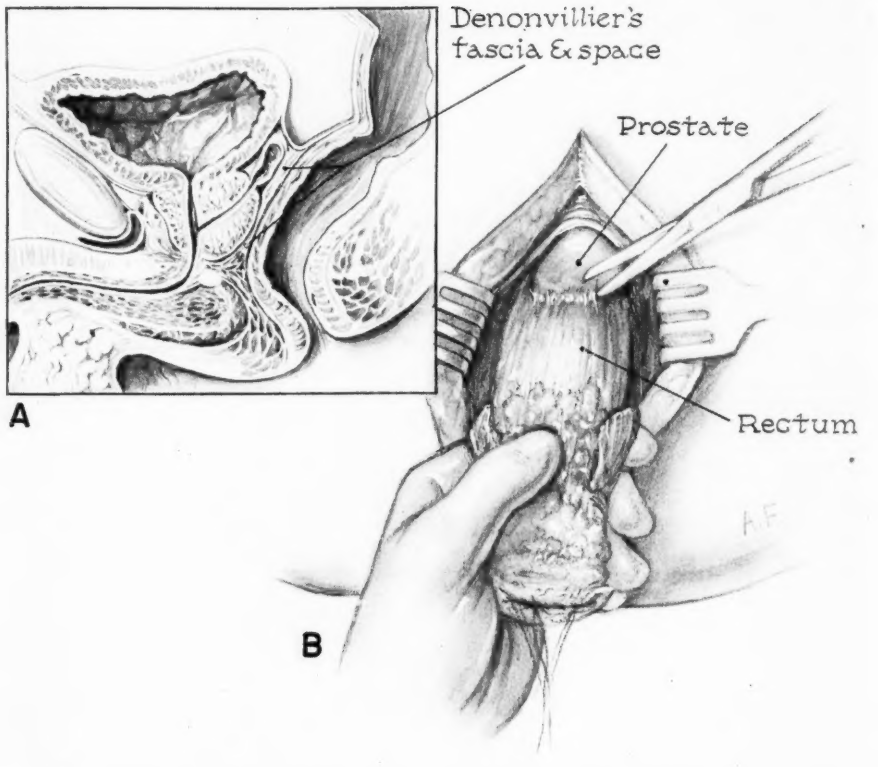


Fig. 2.—Dissection of prostate from rectum anteriorly. Insert shows the location of Denonvillier's space between the prostate and anterior rectal wall.

inal operation. Any so-called uncontrollable bleeding is almost always from pelvic wall veins or insignificant small arteries and can be completely suppressed by pressure packing. Active bleeding is not present because the larger vessels are in the mesorectum and this structure has not been interfered with throughout the dissection.

At the completion of the perineal stage, the ischiorectal space and hollow of the pelvis are thoroughly cleared of liquid and clotted blood and the rectum is placed in a rubber glove. This is tied on with a few turns of heavy silk, and the whole mass is pushed upward into the pelvic space. The perineum is closed by approximating skin and subcutaneous tissues with several interrupted black nonabsorbable surgical (silk) Stewart sutures, allowing room posteriorly for a piece of rubber tubing for drainage.

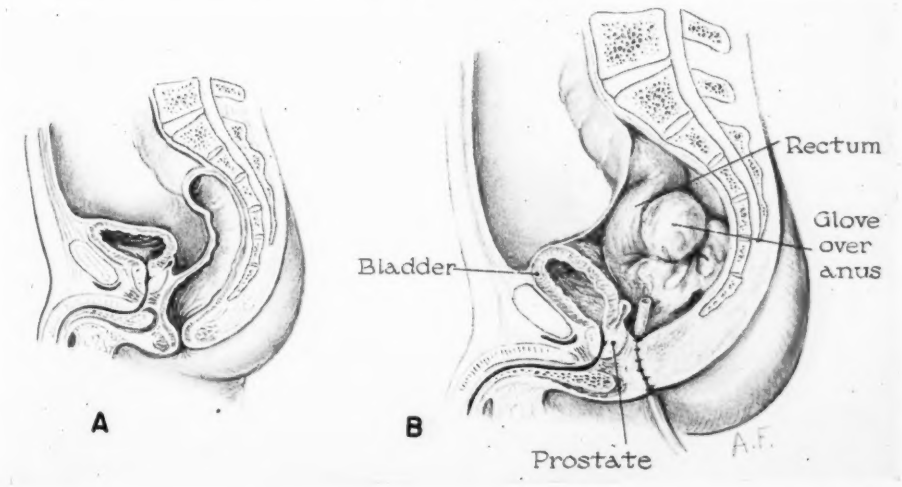
Abdominal Operation.—The patient is removed from the lithotomy position, the legs are slowly extended, and the patient is left in this recumbent position until the completion of the operation. A high Trendelenberg position is unnecessary, since all organs are now at a higher level due to the perineal rectal mobilization.

Incision.—One of two incisions is employed, depending on where the surgeon wishes to place the colostomy. One is a subumbilical incision in the midline extending upward and slightly to the left of the umbilicus, if the surgeon desires to place the colostomy on the left side of the abdomen through a separate counter incision. How-

ever, our choice is the second one, a left rectus incision in the lower abdominal wall. Our preference is based on the fact that (1) the colostomy may be made quickly by placing the mobilized distal rectum and colon in the upper angle of the wound; (2) the colon does not require sectioning for the colostomy until after the abdominal incision is completely closed, thus avoiding peritoneal contamination and also delivery of an open stoma through the counter incision, and (3) a left rectus incision is more suitable for extension proximally, even up to the left costal margin if necessary, if one wishes to mobilize the left colon for a greater distance. This additional length of incision may be preferred in order to dissect more of the mesentery with the inferior mesenteric vessels and their accompanying glands.

Operation. — After the peritoneum is opened, a quick exploration is made of the upper abdomen to detect the presence or absence of metastases in the liver. At the same time, the gall bladder and gastroduodenal region are inspected. The loops of intestine are now packed away from the pelvis, aided if necessary by the Trendelenberg position. A thorough search is made in the pelvis for involved glands, especially along the mesentery of the large intestine. Now it is readily seen that no longer are the pelvic organs located at a low level at the bottom of the pelvis, but, instead, the bladder, uterus, and other pelvic viscera have been pushed upward into the peritoneal cavity and within easy reach of dissection (Fig. 3). The deep acute angle between bladder and rectum in the male patient or the posterior cul-de-sac in the female patient has disappeared, giving a flat appearance to the floor of the pelvis, the latter being now at a higher level. The usual "U-shaped" peritoneal incision is now made around the sides of the rectum, with extensions toward the bladder in front. The pelvic cavity is first entered behind the rectum, since a large space has resulted here from the forward displacement of the rectum by the perineal dissection. In quick order a finger is inserted under the peritoneum on either side of the rectum, and the peritoneum is incised. It is a simple matter to connect

Fig. 3.—Sagittal section drawings to demonstrate altered anatomy of pelvic organs resulting from preliminary rectal mobilization. *A*, before rectal mobilization. Note depth of fossae between posterior aspect of bladder and anterior surface of rectum. *B*, after rectal mobilization. Freed rectum with glove tied over anus, lying in a large retroperitoneal space. Deep fossae have been eliminated resulting in a flattened surface to pelvic floor, at a higher level. Bladder is pushed upward with the dissection, and rectum is displaced forward.



both lateral incisions anteriorly, thus immediately opening up the entire pelvic space. Only a small quantity of extravasated blood is encountered here, since practically all of it has been evacuated in the perineal dissection. The remaining blood is permitted to drain out along the perineal rubber tubing after the completion of the perineal operation. The only remaining rectal attachments are the rectal stalks, and these can be lifted up easily under a finger, sectioned, and ligated. The completely mobilized rectum may be removed gently out of the pelvis, packed into a Davol rubber bag, and placed upon the abdominal wall. The pelvic cavity is sponged as dry as possible while an inspection is made for bleeding points. Should there be considerable general oozing or even hemorrhage from torn veins on the lateral pelvic walls that was overlooked in the perineal procedure, it is possible now to effect hemostasis by ligatures or by pressure packing. In one of our cases we were unable to control diffuse bleeding from pelvic wall veins by the usual methods of clamp and ligature. Thereupon the pelvis was thoroughly packed with wide gauze, and at the end of the operation one end of the gauze was drawn through the perineal wound for later identification and removal from below. Such packs are harmless, many surgeons even using them by choice, believing that they also serve to fill the hollow of the pelvis temporarily and thus support the reconstructed pelvic floor.

The next step is peritonealization of the pelvis, a procedure which can now be done with ease, since the rectum and its tumor are missing. In addition, the peritoneum is lax and mobile after the perineal dissection, all of which permits complete approximation. In many cases, however, it is advisable to use the uterus to insure more complete coverage.

The sigmoid colon is further freed from its attachment to the iliac fossa and to the posterior abdominal wall, and the site on the colon is selected for amputation with the view toward leaving an adequate amount of colon outside the abdomen for a colostomy. The corresponding level of mesentery is now sectioned between clamps and ligated, with no special technique of securing the inferior mesenteric vessels, as is employed in the Miles operation. One can safeguard the viability of the length of colon entering into the proposed colostomy by simply tracing and preserving the arterial arcades proximal to the level of the colon to be sectioned. Penrose drains are placed into the pelvis, emerging through the lower angle of the wound. After closing the peritoneum with chromic catgut the abdominal wall is sutured with "far and near" stainless steel wire sutures. After the insertion of Michel skin clips, the colon is sectioned between Di Martel clamps, one clamp remaining on the colostomy to be incorporated in the dressing. No sutures are used to fix the colostomy to the wound. A collar of petrolatum gauze is placed snugly under the Di Martel clamp, permitting about 2 in. of the colon to protrude above the skin surface in order to prevent later retraction.

Management of Adherent Tumors.—Carcinomas that attach themselves to adjacent viscera are easier to dissect free if the abdominal operation follows the perineal stage. Such tumor masses have considerable surrounding inflammation and most frequently involve the bladder, the uterus, and in many instances loops of small intestine. Since the dissection on the perineal side does not extend upward into the peritoneal cavity, one need not fear any trauma to adherent intra-abdominal organs during the first stage of the perineoabdominal operation. In fact, after the peritoneal cavity is opened, the separation of such tumors becomes much easier than if the dissection were begun in the abdomen, as in the combined operation of Miles. This improvement in the technique becomes evident as one sees that no longer is it necessary to work in depth in the pelvis, the revised pelvic floor being now at a higher level with good exposure and easy accessibility. The attachments of a tumor to the bladder are clearly seen and readily dis-

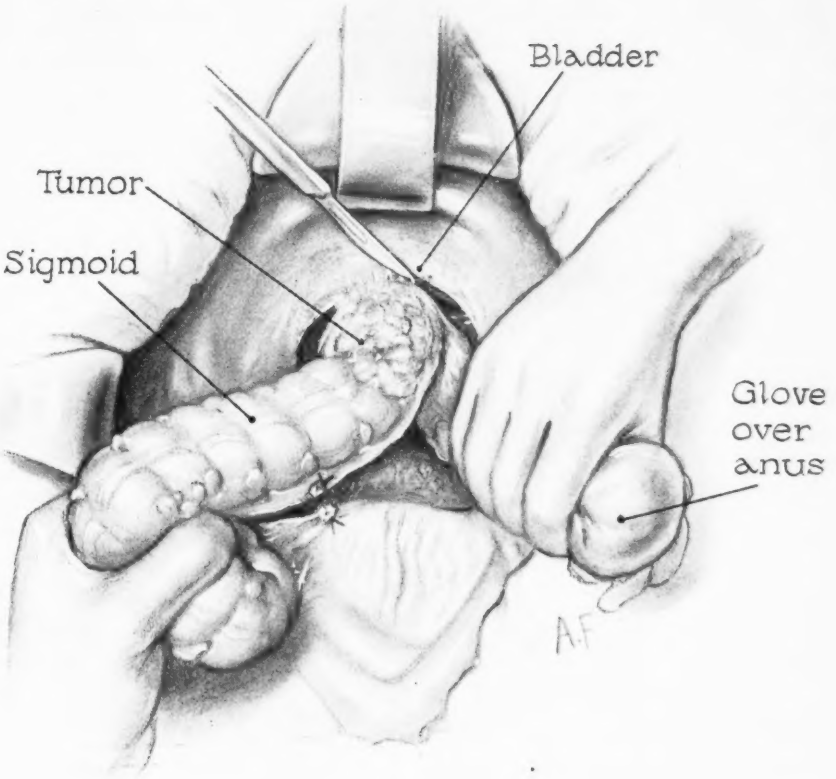


Fig. 4.—Adherent tumors. Using the distal segment of rectum as a handle, the operator lifts the bladder with attached rectal tumor out of the pelvis for better visualization and dissection.

sected free, even if a portion of bladder wall must be removed with the growth in order to accomplish this. The bladder opening is within clear view of the surgeon at all times, thus permitting the edges to be approximated and inverted. A Foley catheter is left in the bladder for at least seven days to permit firm healing. The inability of patients to void postoperatively may be due not so much to trauma of the hypogastric plexus but to edema of the bladder and its surrounding tissues from the dissection.

In one of our cases where the tumor was incorporated in a large inflammatory mass and adherent to the bladder, it was almost impossible to find a cleavage plane, even with the help contributed by a satisfactory perineal dissection. The thought then occurred to us that, if the pelvic space were entered at the outset, before dissecting the tumor, the rectum distal to the tumor could be delivered and used as a handle to elevate the growth and its attached bladder into the wound (Fig. 4). Thereupon, the first step was the entering of the pelvic space behind the rectum by incising the peritoneum laterally on both sides as far as the bladder in front. Then, after the rectal stalks were sectioned, the anorectal region covered by the rubber glove was removed from the pelvis.

By gently lifting the distal rectal segment and moving it in every direction, we were able to see clearly the complete attachment

of the rectum and its tumor to the bladder. In this manner the bladder was delivered even farther upward into the wound by traction on the rectum to either side of the tumor. After separation, a bladder defect low down on the posterior wall was discovered, a defect which may have escaped detection if the bladder were not displaced upward by previous perineal dissection. Therefore, this complication was successfully treated by making use of two procedures: (1) the upward displacement of the bladder into the abdominal cavity, a result achieved by freeing the rectum at the outset by reversing the usual steps of the combined operation, and (2) making traction on the already mobilized rectal segment distal to the tumor to visualize the attachment of the tumor to the bladder.

EXPERIENCES WITH PERINEOABDOMINAL OPERATIONS

Thus far 17 patients have been operated upon, with no mortality. Five were women, and twelve were men. The youngest patient was 43 years of age and the oldest 73. In none of these patients was it necessary to terminate the operation before completion of all the planned steps, indicating a favorable selection of cases for this operation. All tumor masses were excised and proper abdominal colostomies made. However, it must be emphasized again that procedures other than perineoabdominal operations were performed for rectal carcinomas during this period of time, especially anterior resections.

A description of cases with unusual and interesting features follows.

CASE 3.—Operation was performed in May, 1953. Perineal phase of operation proceeded smoothly until the dissection of the prostate from the rectum. A mistake was made in believing that the prostate was part of the rectal tumor. This resulted in a separation of the prostate anterior to the apex and not posteriorly. This error was accounted for by the fact that the tumor mass was in close proximity to the prostate. However, the error was soon discovered, Denonvillier's space was entered and the prostate separated anteriorly from the rectum with ease.

Comment.—With increased experience the dissection plane between prostate and rectum has been more easily discovered. Side-to-side palpation with the fingers will identify the prostate with more certainty and permit the surgeon to enter Denonvillier's space with more assurance.

CASE 4.—Operation was performed on July 22, 1953. Incision and start of rectal mobilization were done in the usual manner. Waldeyer's fascia was entered in front of the coccyx, but severe bleeding was encountered from the middle sacral artery. This was controlled by clamping and suture ligation.

Comment.—After this experience of middle sacral artery hemorrhage an effort was made in subsequent operations not to dissect the rectum with its mesentery too closely from the periosteum. Finger dissection is less apt to traumatize this vessel than the use of instruments.

CASE 10.—Operation was performed on Feb. 3, 1954. This patient was 73 years old, a diabetic and cardiac patient. When the abdomen was opened at the beginning of the second stage, a large inflammatory mass was seen firmly adherent to the bladder. Immediately the peritoneum surrounding the rectum was incised and the dissection begun. Anteriorly, near the bladder, about 2 oz. of green-yellow pus was encountered, evidently from the rupture of an abscess between the bladder and rectum. In order to facilitate the dissection, the distal segment of rectum was delivered out of the pelvis, and by traction upon this and the proximal portion of rectum the connections of the tumor to the bladder were well visualized and subsequently separated. The two segments of rectum acted as handles, and by manipulating them ready access to all portions of the fixed mass was provided. It was a simple matter to separate the tumor from the bladder and to visualize clearly the bladder defect. The bladder opening was easy to repair by infolding with sutures.

This case also presented some difficulty in seeing the attachment of the prostate to the rectum. However, the reason was clear in that there still remained some uncut levator ani muscle fibers. This demonstrated the need for complete and thorough levator ani sectioning before approaching the anterior region of the rectum for separation of the prostate.

Comment.—The maneuver of utilizing the distal rectal segment for bladder dissection will enable the surgeon to extirpate many rectal carcinomas that otherwise seem non-

resectable. Attention is also called to the need for a clean division of all levator muscle fibers stretching from rectum to pelvic wall, before commencing the separation of the prostate from the rectum.

CASE 13.—A 48-year-old man was operated on March 3, 1954. His was the largest carcinomatous mass in the series. The separation of the prostate was accomplished with great difficulty, since the tumor involved the rectum at this level. The prostate must have been traumatized, because there was blood oozing from the urethra.

Comment.—The important feature of this case was the large size of the tumor which at first glance seemed impossible of separation. However, the opinion prevailed that, were it not for the preliminary mobilization of the rectum in the perineal stage, the removal of such a large-sized tumor would have been impossible.

CASE 14.—A 54-year-old woman was operated on March 26, 1954. Hers was another huge carcinoma mass fixed to the right lateral pelvic wall. Separation was difficult in this region because of unusual adhesions involving the upper rectum resulting in bleeding from pelvic wall veins. The dissection was therefore terminated from the perineal side and the abdomen opened. As the peritoneum was being incised around the rectum, a ureter was seen adherent to the tumor. This was dissected off with ease, since everything was elevated out of the pelvis in clear view owing to the preliminary perineal mobilization. In addition, after the rectum was brought out of the pelvis, bleeding was still profuse from the lateral pelvic veins. A large mass of gauze packing was inserted into the pelvic space, and the bleeding was promptly controlled. Peritonealization and the other operative steps were completed and the abdomen closed. Before the patient left the operating table, one end of the gauze packing was delivered through the perineal wound for about 2 in. to permit easy withdrawal from below at a later date.

Comment.—This case taught several lessons:

1. If the higher rectal dissection from the perineal side seems to be too difficult and too traumatizing, one should discontinue the perineal phase and proceed immediately to the abdominal stage, lest too much trauma be caused.

2. If the rectal mobilization is done first, even a structure such as a ureter is more easily visualized and dissected free from the tumor mass in the abdominal stage.

3. Active bleeding from pelvic veins, resulting particularly from large adherent tumors, requires firm gauze packing in the pelvic space, to be removed a few days later through the perineal wound.

SUMMARY AND CONCLUSIONS

The Miles combined abdominoperineal operation is in principle the best procedure thus far for the radical treatment of carcinoma of the rectum. Ofttimes, it may be difficult of accomplishment, time consuming, and shocking.

The perineoabdominal approach, as presented in this report, reverses the order of the two stages, with the operator performing the perineal stage first.

The abdominal stage of the perineoabdominal operation becomes easier and consumes less time, leaving only two steps to complete the operation: the incision around the rectum through the pelvic peritoneum and the sectioning of the rectal stalks.

The altered anatomy of the pelvis is discussed to show how the prior mobilization of the rectum converts the abdominal procedure from an operation in the depth of the pelvis to one at a higher level with all structures easily accessible.

The perineoabdominal operation also has an advantage in patients with large inflammatory tumors, in obese patients, and in persons with large intestinal loops resulting from partial intestinal obstruction.

The perineoabdominal procedure is a more aseptic operation because the sectioning of the rectum with its contaminating fecal lumina is eliminated.

Anesthesia in these operations contributes less shock than when the abdomen is opened first, as in the Miles operation, since less anesthetic is required in perineoabdominal operations, whether spinal or inhalation anesthesia is used.

A description of the operation is presented with emphasis placed upon the advantages of limiting the perineal dissection to the space below the rectal stalks and the peri-

toneum, saving this last step for the abdominal operation. In this manner extravasated blood and infectious material resulting from mobilizing the rectum do not contaminate the clean peritoneal cavity before the surgeon has an opportunity to isolate the pelvic field after opening the abdomen from above.

Reasons are also advanced for the impracticability of using the "two-team method" for operating upon cancer of the rectum in the average hospital, especially because of the problem of limited personnel.

The perineoabdominal operation as presented in this report is based upon a study of 17 patients selected for this procedure and operated upon without mortality. A brief summary is given of individual cases that showed unusual features. In our opinion this operation in selected cases of extraperitoneal rectal carcinoma seems to be an improvement over the Miles operation and at least as effective in eradicating the disease.

75-17 41 Ave.

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Acute Pneumocholecystitis

A Review and Report of Two Cases

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Acute pneumocholecystitis or acute gaseous cholecystitis is a descriptive term for an acutely inflamed and sometimes gangrenous gall bladder whose lumen contains air. Occasionally it is characterized by pericholecystic air infiltration. Pyopneumocholecystitis is characterized by a fluid level. Similar to cholecystitis, with or without cholelithiasis, the pathogenesis of pneumocholecystitis is a decrease in the local resistance of the gall-bladder wall, which allows a previously avirulent gas-producing organism to become virulent and results in growth of the organism in the wall and within the gall bladder. Production of gas follows within the lumen of the gall bladder. The mechanism whereby gas infiltrates the pericholecystic tissue is not definitely established. There are two theories. One assumption is that air, initially in the lumen, finds its way into the pericholecystic tissues by way of local areas of necrosis in the mucosa and submucosa owing to the virulent inflammatory process. The other conception is that the normal Rokitansky-Aschoff sinuses, which are peculiar out-pocketings of the gall bladder mucosa extending into the muscularis and which in the normal gall bladder are potential pathways for air, actually are in the diseased gall-bladder true pathways, whereby air reaches the pericholecystic tissue. We can be content to say that pericholecystic air infiltration is a definite often observed phenomenon in acute pneumocholecystitis.

The pathology of acute pneumocholecystitis does not differ characteristically from the pathology of cholecystitis. Varied degrees of inflammation have been observed where only the mucosa is involved and more frequently where the entire wall of the gall bladder is involved in the inflammatory process. Cholelithiasis does not necessarily accompany the inflammatory process. The inflammatory process in acute pneumocholecystitis is undoubtedly severer and the organisms apparently are more virulent because the incidence of gangrene of the gall bladder with perforation is high. The differential diagnosis of this disease should include perforated peptic ulcer, acute pancreatitis, pneumonia, and perinephritic abscesses with gas-producing bacteria. In the first case presented in this paper, the differential diagnosis of amebic abscess had to be seriously considered because of the patient's four previous admissions for diarrhea, cause of which was undetermined.

Of historical interest, Stolz [1] in 1901, reported three cases at autopsy in which gas was found in the gall bladder and biliary ducts. Whether these represent acute pneumocholecystitis by our definition can be disputed. Bell, Brown, and Lenhardt [2] in their review in 1953 do not include these cases in the 27 cases reported. Lobinger [3] in 1908 reported a case in which gas was found in the gall bladder at the time of cholecystectomy, with recovery of the patient. Halle and Marguézy [4] reported a case in the French literature in 1922 of gangrenous cholecystitis in which a pure culture of Clostridium welchii was obtained. Other

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cases have since been reported, and reference can be made to the collective review by Bell, Brown, and Lenhardt in 1953. In 1931, Hegner [5] reported the first case that was diagnosed preoperatively by x-ray examination. Bell, Brown, and Lenhardt state in their review that the majority were between 50 and 70 years of age and 60% were men. They also found that 30% of the cases were diabetic to some degree. The organisms which have been identified in cultures taken from the surgical specimen or from pus contained in the gall bladder are C. welchii, Escherichia coli, streptococci, both aerobic and anaerobic, and Staphylococcus albus. In only 9%, however, was C. welchii cultured. The diagnosis of acute pneumocholecystitis from a clinical appraisal is the same as acute cholecystitis. The patient is usually rather ill, with epigastric or right upper quadrant pain. Nausea and vomiting are common. Very often there is a previous history of symptoms referable to biliary-tract disease. Tenderness is localized in the right upper quadrant, and in about one-half of the cases a mass is palpable just below the right subcostal border. The final diagnosis is made by characteristic x-ray appearance. This characteristic appearance can usually be differentiated from that of gas in the bowel by its configuration and high location in the right upper quadrant. When pus is present along with the air, characteristic fluid levels will be noted in the upright and lateral decubitus views. However, the mere presence of gas in the gall bladder does not make the unequivocal diagnosis. Abel and Rousselot [6] point out that gas may enter the biliary system in others ways: (1) by means of a fistula between the biliary tree and the gastrointestinal tract and (2) an incompetent sphincter of Oddi. The differentiation is usually not difficult, for the biliary ducts will also be filled with air and the gall bladder may not be visualized.

The purpose of this paper is to report two additional authenticated cases and to emphasize four points: (1) the value of abdominal x-ray films, including upright and lateral decubitus views, in cases of suspected cholecystitis; (2) the urgent need for prompt surgery once the diagnosis of acute pneumocholecystitis is made; (3) cholangiograms in the early postoperative period in those cases in which cholecystostomy was performed, and (4) postoperative follow-up of the patients, including intravenous visualization of the biliary ductal system to rule out retained calculi.

The treatment of this disease process has in the past been both medical and surgical. It is felt that the very nature of the disease predisposes to imminent gangrene and rupture of the gall bladder. The operation of choice, whether cholecystectomy or cholecystostomy, should be a decision based on the peculiar findings at the time of surgery.

REPORT OF CASES

CASE 1.—A 64-year-old white man was admitted to the Veterans Administration Hospital, Hines, Ill. on April 25, 1955, complaining of chills, fever, nausea, vomiting, and right-upper-quadrant pain. These symptoms had been present for four days prior to admission to the hospital. The patient described his pain as constant in nature. His pain was recurrent along with nausea and vomiting and persisted until the time of admission.

Past History.—This patient admitted that for many years prior to the present illness he had intermittent mild episodes of vague epigastric distress associated with bloating and eructation and a selective food dyspepsia for fried and fatty foods. This patient had four previous admissions to this hospital with a diagnosis of diarrhea, cause undetermined, on each admission. Complete work-ups each time were completely negative as to the cause of the diarrhea. On the patient's second hospital admission, however, work-up did reveal the suggestion of pancreatic disease based upon an x-ray revealing a widened duodenal sweep. During this admission, the patient had an exploratory laparotomy, and exploration of the abdomen at that time was entirely normal, except for a fusiform aortic aneurism which was found in the region of the celiac axis and superior mesenteric arteries. The pancreas itself was normal. No treatment referable to the aneurysm was rendered. No stones were palpated in the gall bladder. His postoperative course was uneventful, except that he did develop heterotopic bone in the abdominal incision.

Physical Examination.—The patient was a well-developed well-nourished but dehydrated white 63-year-old man who appeared acutely ill. His temperature was 100 F, pulse rate 100, and respiration

Fig. 1.—X-ray demonstrating fluid level and pericholecystic gas.

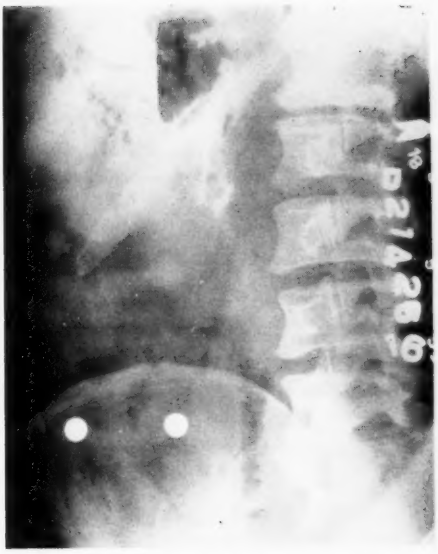

Fig. 2.—Decubitus view of patient shown in Figure 1.

rate 24. His blood pressure was 170/100. He appeared slightly anemic. There were Grade III arteriosclerotic changes in the retina. The heart was enlarged to the left, but there were no murmurs. There was no peripheral edema. Examination of the abdomen revealed marked guarding and rigidity in the upper abdomen. There was exquisite point tenderness in the right midsubcostal region, with rebound tenderness also localized to the right subcostal region. No masses could be palpated on the admission examination. The peripheral pulses, particularly the dorsal pedis, were difficult to obtain. The feet, however, did not feel cold. The remainder of the physical examination was within normal limits.

Laboratory Data.—Laboratory examination revealed that on the day of admission the patient's white blood cell count was 32,000, with 81% neutrophiles and 19% lymphocytes. The red blood cell count was 3,650,000, with 11 gm. of hemoglobin. Serum amylase was 16 Somogyi units. Bleeding and coagulation times were normal. Urinalysis revealed a trace of albumin and 2+ sugar. There were 8 white blood cells per high-power field and 1 red blood cell per high-power field. On the day after admission, the patient's white blood cell count was 18,200, with 93% neutrophiles and 7% lymphocytes. Electrolyte studies obtained on the day after admission revealed a sodium level of 137 mEq/L, potassium 4.15 mEq/L., carbon dioxide 23 mEq/L,

Fig. 3.—Appearance of completely gangrenous gall bladder.

Fig. 4.—Cholangiogram through sinus tract, demonstrating absence of calculi.

and chlorides 109 mEq/L. The nonprotein nitrogen was 33.7 mg/100 cc. On the second day of hospitalization, the serum bilirubin was 0.8 unit, alkaline phosphatase 5.4 units, and thymol turbidity 3.4 units. Serology was negative. Total cholesterol was 172 mg/100 cc. On the day of admission, an x-ray of the kidney, ureter, and bladder was obtained, and interpretation of this x-ray showed no evidence of obstruction or radiolucent calculi. An upper gastrointestinal x-ray and a cholecystogram were obtained. The gall bladder did not visualize on the cholecystogram; however, there was noted a large, roughly rounded, 8 cm. in diameter, mottled, irregular, radiolucent shadow in the projection of the liver, which demonstrated a fluid level on the lateral decubitus view (Figs. 1 and 2). The upper gastrointestinal x-ray was reported as essentially normal. An electrocardiogram showed left ventricular strain. The chest x-ray revealed moderate cardiac enlargement and a high right diaphragm.

Fig. 5 (Case 2).—Appearance of x-ray showing pericholecystic air.

Fig. 6 (Case 2).—Appearance of x-ray showing pericholecystic air.

Hospital Course.—On admission to the hospital it was believed that the patient had acute cholecystitis, and it was decided that conservative therapy was the indicated treatment of choice. The peritoneal reaction began to subside, after which it was possible to palpate a mass in the right upper quadrant. This well-localized mass remained tender to palpation. The patient became ambulatory. However, he still persisted in having right upper quadrant pain of a mild nature. Upon completion of the x-ray studies, it was decided that surgical intervention was indicated. The preoperative diagnosis was acute pneumocholecystitis. The patient was operated upon through a right subcostal incision. When the peri-

toneum was opened, a large, firm, indurated mass was noted just below the liver. This mass was covered with attached omentum. After this omental flap was freed, the tense wall of the gall bladder could be seen. This was punctured with an 18-gauge needle, and thick, yellow pus was aspirated along with air. The hole in the dome of the gall bladder was enlarged with a curved forceps and all the pus was evacuated from the gall-bladder lumen. After aspiration of the gall bladder, a long curved forceps was introduced into the cavity and a gangrenous, somewhat gelatinous cast of the gall bladder (Fig. 3) was removed with ease. The resultant space was drained with two large Penrose drains, as was the right lateral peritoneal gutter. The patient's immediate and eventual postoperative course was entirely benign. Culture of the pus obtained from the gall-bladder lumen revealed C. welchii. The drains were left in for a period of approximately 10 days. On the 12th day, 30 cc. of 70% iodopyracet (Diodrast) was injected into the draining site and a cholangiogram was obtained (Fig. 4). All drainage had subsided from the site of the stab wound and the wound was clean and healed in two weeks. A cholecystogram obtained three weeks after surgery revealed nonvisualization of the gall bladder.

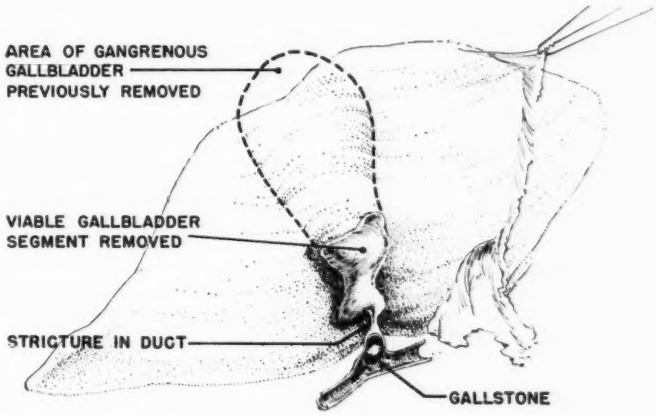

Fig. 7.—Diagram of pathology noted during second operation.

Case 2.—A 65-year-old white man was admitted to the hospital complaining of severe generalized abdominal pain of a few hours' duration. The pain was constant, with some localization in the right lower quadrant.

Past History.—This patient had been treated two weeks previously for an acute cholecystitis. At this time he had right upper quadrant pain and tenderness and a spiking temperature up to 103 F for one week's duration. His pain and temperature subsided, and he left the hospital feeling well.

Physical Examination.—The patient was a well-developed white man acutely ill. His temperature was 101 F, and his blood pressure was 140/78. He was perspiring profusely and had the typical tremors of Parkinson's disease. The abdomen was diffusely tender and rigid, with increased tenderness in the right lower quadrant. Bowel sounds were absent.

Laboratory Data.—The urine examination was normal. The white blood cell count was 25,000 with 91% neutrophiles. The x-rays on the previous admission were reviewed, revealing the gall-bladder area outlined by air (Figs. 5 and 6).

Hospital Course.—The patient was operated upon with a preoperative diagnosis of rupture of the gall bladder. The abdomen contained free bile. The omentum was adherent to the gall-bladder area. As this was separated, the gangreous gall bladder was visualized. This was removed with a tissue forceps and was similar in appearance to Figure 3. The area of the gall bladder and the right gutter were drained with Penrose drains. These drains were left in place for 10 days. The biliary fistula closed five days later.

Nine months later, this patient developed biliary colic and jaundice. At the indicated time, this patient was reoperated upon and a stone removed from the common duct. The pathology noted is shown in Figure 7.

SUMMARY

Pneumocholecystitis is an unusual manifestation of acute cholecystitis which can be diagnosed by x-ray of the abdomen. Careful examination is necessary and operation during the acute phase may be indicated because of potential rupture of the gall bladder. A cholangiogram through the biliary fistula

can be of value in diagnosing residual biliary pathology. Cultures at the time of surgery are important because of the high incidence and variety of organisms encountered in this disease.

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Improved Apparatus for Halter Traction

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An increasing number of patients with ruptured disc of the neck and "whiplash" injury are being treated by halter traction.

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For this purpose a device which can be readily adjusted to give reasonably accurate, measurable increments of pull, which is simple to set up and to use, and which is completely under the control of the patient is highly desirable.

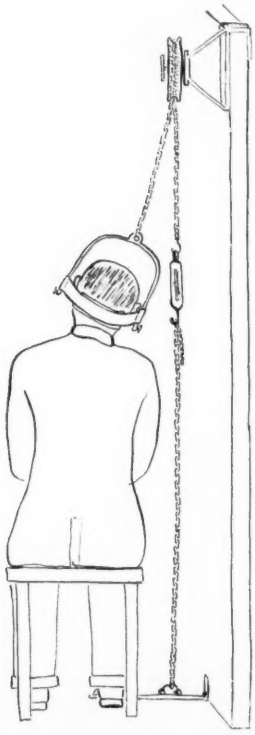
Consistently good results can be expected only if the attending physician has an apparatus that he can depend upon to give the

Figure 1

Figure 2

Figure 3

Figure 4



pull he prescribes. For many afflictions of the neck it has been found that 25 lb. of vertical traction is the minimum required to produce symptomatic relief. Yet, the small 1- to 2-in. pulleys generally in use have been found by actual test to be 10% to 50% erratic. The smaller the pulley, the less dependable it was. The troughs or grooves of these small pulleys were often so narrow as to cause heavy friction. According to the way the traction was set up, this friction could increase or decrease the desired poundage. In one case a rope was passed over a commonly used pulley arrangement with

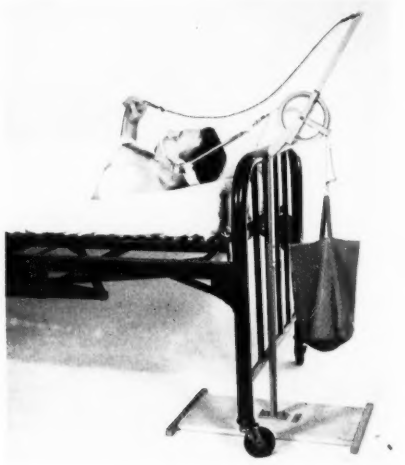


Figure 5

10 lb. on one end and 20 on the other. The friction of the wheel prevented any motion, although the weight on one end was twice that on the other. First of all, then, a large, 6-in., pulley has been designed, with a wide groove, which has proved more satisfactory.

To keep the device both easy to operate and portable, a simple apparatus appliable to a door (Fig. 1) was developed with the assistance of several orthopedists and neurosurgeons. It consists of a large wheel attached to a steel bar which has a grooved sleeve which slides over the top of the door. Through this wheel a small link chain is

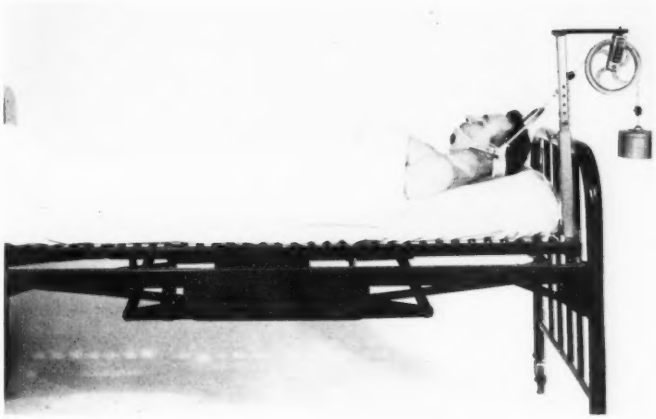


Figure 6

passed—a chain because it will not stretch and the apparatus once adjusted to a particular patient will stay adjusted. On one end of this chain is an iron yoke to which is stitched an occipital band and a chin band, lined with sponge rubber. These are detachable and for cleanliness sake may be covered with fresh stockinet. The other end of the chain is attached to a steel bar which also has a sleeve which slides under the bottom of the door. The bar is hinged at the sleeve, and as the chain is shortened, simply by hooking successive links to a hook on the spring scale interposed at eye level, the patient produces his own pull by stepping down on the bar. It is a comfort to the apprehensive patient to know that he can release the pull at any moment without assistance. Furthermore, in the event that a patient should faint, as the leg muscles become limp the upright position is no longer forcibly maintained. As for portability, the whole apparatus can be fitted into a small brief case. For doctors' offices, on the other hand, a chair device, such as shown in Figure 2, may be preferable.

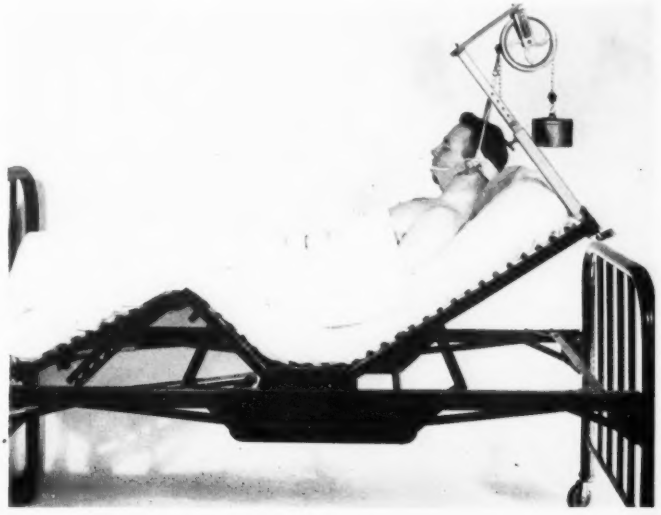


Figure 7

Another feature of this versatile apparatus is that the patient can be taught to produce pull on the head and neck in various attitudes and at various angles, should it be desired. The muscles and tendons of the neck run at angles, as shown in Figure 3. Should it be desired to create pull in the direction of the fibers of these muscles, so as to stretch them, then it is possible to have the patient position his head so that the pull will be created lengthwise of the oblique muscles, as shown in Figure 4. With use of a variety of positions, stretch of all the cervical muscles may be encompassed.

Apparatuses for bed traction, incorporating the same principles of the large wheel and self-management, have also been developed. A type adaptable to any bed, even a "Hollywood" bed, is shown in Figure 5. Still another type, which attaches to the springs of a hospital bed, is shown in Figures 6 and 7.

Apparatus is available at The Spinks Company, 584 Manford Road, Southwest, Atlanta, Ga.

Functional Efferent Stomal Obstruction Following Subtotal Gastric Resection

A Report of Two Cases Demonstrating the Role of Hypersecretion and Hyperacidity

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INTRODUCTION

Efferent stomal obstruction is an occasional complication of subtotal gastric resection, even when the procedure is carefully planned and executed. The forbearance of surgeon and patient is usually severely strained before the situation is resolved, and the postoperative management is a real challenge to good surgical judgment.

Since there is no unanimity of opinion with regard to the exact etiology of this complication, we believe that any new observations should be reported. We have observed two cases in which hypersecretion and hyperacidity were present and measures directed toward the suppression of these factors apparently resulted in release of the obstruction.

REPORT OF CASES

CASE 1 (Fig. 1).—A man of 50 years had had periodic episodes of burning, gnawing epigastric distress occurring one or two hours after meals and at night, for 12 years prior to his initial examination, in 1949. Roentgenologic examination of the upper gastrointestinal tract revealed an ulcer crater on the posterior wall of the first portion of the duodenum. The patient was instructed thoroughly, and an adequate program of medical therapy was outlined. In the ensuing four years he sporadically followed instructions but in the main ignored them. In March, 1953, his epigastric distress changed in character, with the pain becoming more intense and radiating through to the back. Alkali and milk no longer produced prompt and complete relief. Roentgenologic examination of the duodenum disclosed a large ulcer crater penetrating posteriorly. A program of strict rest and rigid ulcer management was followed for four weeks without producing any control of his pain; therefore, on Aug. 14, 1953, laparotomy was performed. Exploration revealed a huge ulcer penetrating into the wall of the gall bladder. Careful dissection allowed removal of the ulcer-bearing area and closure of the duodenal stump. Subtotal gastric resection was then performed, removing all of the lesser curvature and at least two-thirds of the greater curvature. After partial closure of the lesser curvature side, gastrointestinal continuity was restored by the performance of a retrocolic isoperistaltic gastrojejunostomy.

The first seven postoperative days were characterized by increasing gastric retention necessitating frequent use of Levin-tube suction. At the end of 11 postoperative days it was obvious that nearly complete efferent stomal obstruction was present and that total parenteral feeding would be required. Quantitative replacement of gastrointestinal fluid loss by intermittent suction and vomiting had prevented the development of metabolic alkalosis but the caloric deficit had been great. A program utilizing the Scribner technique[16] was instituted. Careful attention to detail permitted the maintenance of fluid and electrolyte balance, and utilization of parenteral fluids containing 10% dextrose and 10% ethyl alcohol permitted caloric intake to exceed 2300 calories in each 24-hour period. On the 12th postoperative day it was noted that the gastric chlorides were markedly elevated and that the urinary chlorides were depressed. (Fig. 1). Additional titration confirmed this observation and led us to test for free and total acid in the aspirated fluid, which revealed surprisingly high concentrations. The volume of aspirated gastrointestinal fluid seemed to be increasing; hence, it was determined to attempt neutralization of the gastric

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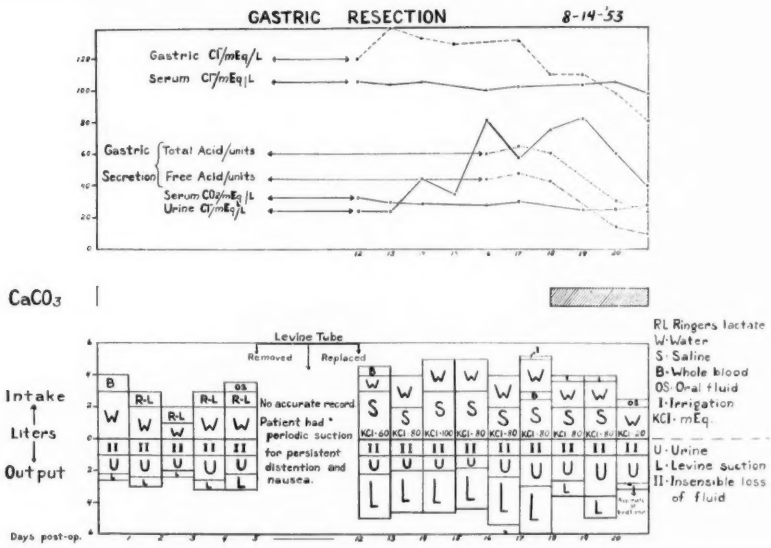

Fig. 1.—Postoperative balance sheet on Case 1. Note reduction in gastric retention following use of $CaCO_3$.

content with alkali in the hope that there was some relationship between the continuing hyperacidity and the chronicity of the obstruction. Accordingly, on the morning of the 18th postoperative day 2.0 gm. of calcium carbonate dissolved in 50 cc. of tap water was injected into the stomach every two hours and the Levin tube was clamped for an hour after each injection. The neutralization of gastric content was not complete, but there was a sharp drop in the volume of aspirated fluid from 3 liters per 24 hours to 1 liter per 24 hours. After three days of alkali therapy the gastric suction was discontinued. The patient tolerated his postgastrectomy diet, and convalescence proceeded without further incident.

Since his operation, the patient has had occasional epigastric discomfort, but only after periods of extreme anxiety regarding his business. One gastric analysis performed about three months after operation revealed 30 units of free acid, and another, one year later, yielded 20 units of free acid. Recent roentgenologic examination showed a normally functioning stoma and no evidence of gastrojejunal ulceration.

Case 2 (Fig. 2).—A 48-year-old man was first seen on Jan. 2, 1955. He had had periodic episodes of epigastric distress for 13 years but had been particularly uncomfortable in the previous 5 weeks. His pain was gnawing in character and located high in the epigastrium. It seemed to occur when his stomach was empty and was particularly severe at night. Prior to the present episode relief had been attained easily with milk or alkali but was now incomplete. Roentgenologic examination of the upper gastrointestinal tract disclosed a constant constriction deformity of the duodenum and an unusally large ulcer crater. A program of rigid ulcer management failed to produce relief of symptoms. On Jan. 18, 1955, his abdomen was explored surgically and he was found to have a huge ulcer penetrating into the head of the pancreas, with marked surrounding edema and induration. Consequently, the ulcer was left in situ, and the duodenal stump was closed. A posterior Hofmeister gastric resection was then performed, removing the entire lesser curvature and two-thirds of the greater curvature.

The postoperative course was uneventful until gastric suction was discontinued on the third day. The patient promptly became distended and nauseated, and he vomited an estimated 600 cc. of bile-stained fluid. A parenteral feeding program utilizing the Scribner technique [16] was initiated the same day. The ensuing four days demonstrated the presence of near-complete efferent stomal obstruction as the volume of gastric aspirate steadily increased. Titrations of this aspirate disclosed high concentrations of free and total acid (Fig. 2). On the morning of the eighth postoperative day, 2.0 gm. of calcium carbonate dissolved in 50 cc. of tap water was injected into the stomach every second hour, and the tube was clamped for one hour after

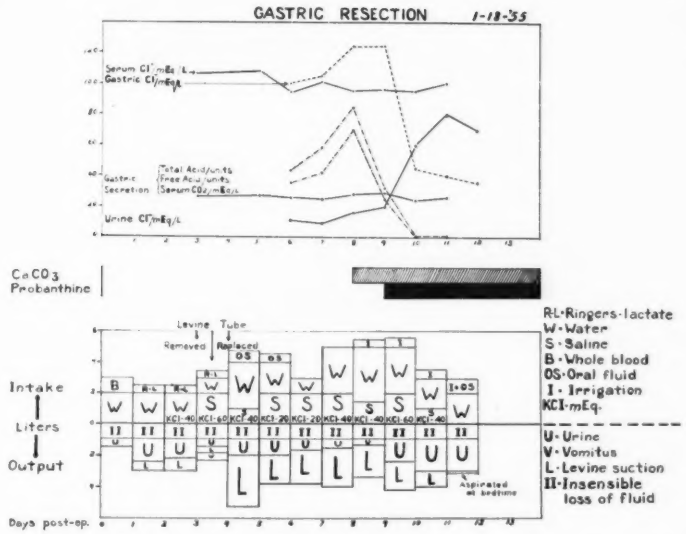

Fig. 2.—Postoperative balance sheet on Case 2. Note rapid reduction in gastric retention following use of $CaCO_3$ and propantheline bromide.

each injection. This resulted in a marked decrease of the acid concentration of the gastric aspirate but not complete neutralization. On the morning of the ninth postoperative day, parenteral injections of propantheline bromide (Pro-Banthine), 15.0 mg. every four hours, were begun, with the hope of further decrease in the volume and acid concentration of gastric secretion. The concentration of acid in the gastric aspirate promptly reached zero values, chloride concentrations in the gastric aspirate dropped from 125 mEq/liter to 45 mEq/liter, and urinary chloride concentrations climbed sharply from 20 mEq/liter to values exceeding 60 mEq/liter. On the 11th postoperative day gastric suction was discontinued and aspiration at bedtime yielded only 200 cc. of gastric content. The patient tolerated his postgastrectomy diet without difficulty, and convalescence proceeded without incident.

The patient is now symptom-free, and a fractional gastric analysis with histamine two months after surgery disclosed the presence of achlorhydria.

COMMENT

Obstruction of the efferent gastroenteric stoma in the immediate postoperative period may be either mechanical or functional. The mechanical factors which have been most frequently implicated are excess cuff formation, adhesions, and herniation of the stoma into the lesser peritoneal sac.† Other less frequent derangements have been reported.‡ Since mechanical obstruction customarily involves both efferent and afferent jejunal loops, it is usually not difficult to differentiate from functional efferent obstruction. The retention fluid contains no bile and symptoms of closed-loop obstruction may develop rapidly. Mechanical obstruction of the efferent loop alone rarely occurs, but, since this is a simple obstruction, differentiation from functional obstruction in cases which do not respond to conservative measures is ordinarily impossible without reexploration.

Many authors § believe edema of the stoma to be the important underlying factor in functional efferent stomal obstruction. Ravdin [14] is of the opinion that a low serum protein accentuates the edema following trauma, and he graphically demonstrated a definite relationship between gastric emptying and serum protein concentration in two cases. Welch [19] concurs in this opinion and believes the complication to be commonest in elderly patients whose chronic pyloric

† References 12, 15, and 17.
‡ References 1, 13, and 18.
§ References 1, 14, 15, 17, 19, 20.

obstruction has resulted in malnutrition and protein deficit. Ebriel and Naftalin [4] made an extensive study of the potassium and sodium concentrations of blood sera in patients subjected to gastric resection. They concluded that potassium depletion and sodium retention were important factors in the development of functional obstruction. Their data suggest that obstruction was prone to develop if the spread between sodium retention and potassium deficit reached 300 mEq. and that this spread need not be of this magnitude if there were a biochemical upset before the operation. They conclude that sodium loss was as important as potassium gain in the treatment. Golden [5] states that the gastric remnant is a distensible bag lacking the peristaltic activity necessary to force its contents into the efferent loop, and he has demonstrated that ingested barium is not delayed at the stoma but is halted by spasm 5 to 7.5 cm. down the efferent loop. Prohaska and co-workers [12] failed to substantiate Golden's observations. They believed that functional obstruction occurred when the efferent loop was not dependent, as is almost always the case in the antiperistaltic anastomosis and is occasionally so after high resection of the greater curvature in the isoperistaltic anastomosis.

The treatment of functional efferent stomal obstruction is conservative and directed toward the maintenance of fluid, electrolyte, and nutritional balance in the expectation that the stoma will spontaneously open.‖ Other measures have been advocated to supplement, if necessary, this basic concept of treatment. Colp and Weinstein [2] have found repeated lavage of the stomach with hot water to be helpful. Sachs [15] has an ingenious method for handling this problem. He places a mercury-weighted bag on the tip of a Levin tube and directs this through the stoma to relieve the obstruction. He reports success in two cases. If, despite conservative therapy, spontaneous release of the obstruction is delayed, surgical exploration should not be postponed until the patient is in extremis, because a mechanical obstruction may be found.¶ If a mechanical obstruction is not found, a simple feeding jejunostomy can be performed which may be lifesaving. Welch [19] limits conservative therapy to one week in elderly patients and two weeks in younger patients before reoperation. At the other extreme Graham # cites a case which was treated conservatively for 43 days before complete obstruction disappeared. Welch [19] performs a double jejunostomy on those patients whom he suspects may become obstructed, and, if they do, he can simply join the two tubes and safely wait for the situation to resolve. Zintel [20] routinely places a double-lumen Abbott-Rawson tube with one end in the stomach and the other in the efferent loop so that gastric suction and simultaneous jejunal feeding can be instituted if necessary. It would be ideal if one could forsee which patients would develop retention in the postoperative period so that a double jejunostomy could be fashioned or a double-lumen Abbott-Rawson tube could be correctly placed at the time of surgery. Unfortunately this is not the case, and the routine use of such devices is not without hazard. Priestley [11] condemns the routine use of continuous postoperative suction and believes that it invites complications.

It is our opinion that the postoperative occurrence of hypersecretion and hyperacidity in two patients with functional obstruction of the efferent loop is more than coincidence. Two references have been found which by inference point to hypersecretion and hyperacidity as factors of importance in the etiology of this complication. Nissen [9] uses large doses of atropine in the early stages of treatment to reduce the volume of secretions, and Prohaska [12] has utilized propantheline bromide for the same purpose. The procedure of subtotal gastric resection markedly suppresses the gastric phase of secretion and

‖ References 2, 9, 12, 14, 17, and 19.

¶ References 1, 2, 8, 9, 12, 13, 17, and 19.

Graham, cited by Maxeiner, S. R.[6]

reduces the cephalic phase,* but this is not always the case, as demonstrated by Noring.[10] In his report of 38 patients subjected to subtotal gastric resections of similar magnitude, there were three persons in whom there was no reduction in the amount of acid or the volume of secretions in the postoperative period. Experimental evidence exists which may explain the occurrence of hypersecretion and hyperacidity in the immediate postoperative period.[7] First, it has been shown in dogs that any surgical procedure in the upper abdomen may frequently be followed by hypersecretion and hyperacidity for a period from a few days to two weeks and that this hypersecretion and hyperacidity may be augmented by the parental administration of saline. Second, it has been demonstrated that there is a portion of the gastric phase of secretion which is not abolished by antral resection. This is a factor of direct mechanical stimulation of the mucosa by distention, which does not require a hormonal mechanism. Third, the intestinal phase of gastric secretion is considered to be of negligible importance in the intact stomach, and its importance following gastric surgery is difficult to assess, but Ivy[7] has theorized that trauma to the jejunal mucosa may result in release of histamine or like substance, with subsequent augmentation of gastric secretion.

It is not inconceivable that this experimental evidence serves to explain at least in part our observations on these two patients. It is probable that interference with the normal muscular activity of the stomach and intestine resulting from trauma at surgery is the initiating factor in functional efferent stomal obstruction, but it is possible that a highly irritating secretion, as demonstrated in our cases, might initiate spasm of the efferent loop, as described by Golden.[5]

SUMMARY

Two cases of efferent stomal obstruction following subtotal gastric resection are presented in which hypersecretion and hyperacidity appear to be factors in the persistence of the obstruction. Suppression of these factors apparently resulted in release of the obstruction. The literature pertaining to the etiology and treatment of stomal obstruction following subtotal gastric resection is briefly reviewed and experimental evidence is cited to explain the appearance of hypersecretion and hyperacidity in the immediate postoperative period. We are hopeful that others, when faced with this problem, will try acid suppression therapy in the treatment of stomal obstruction when it is discovered that there is associated hyperacidity.

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Hemocholecyst Following Ruptured Aneurysm of Portal Vein

Report of a Case

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Hemorrhage into the biliary tract, commonly referred to as hemobilia, may produce a hemocholecyst, which may be manifested by abdominal pain, jaundice, and a distended gall bladder. As the case to be presented illustrates, a hemocholecyst associated with jaundice can conform with the clinical features of Courvoisier's law.

Intracholedochal hemorrhage, or a hemocholecyst, may develop after or in association with (1) trauma, inflammatory lesions, or neoplasms of the liver [1]; (2) trauma, neoplasm, intracholedochal intubation,[2] or parasitic infestation of the extrahepatic bile ducts; (3) cholecystitis, cholelithiasis,[3] hematoma,[1] neoplasms,[4] or apoplexy of the gall bladder [5]; (4) penetration or reflux hemorrhage from a duodenal ulcer [6]; (5) duodenal, ampullary, or pancreatic neoplasms, or (6) rupture of an aneurysm of the hepatic [7] or cystic artery.[8]

The probable sequence of events in the following case of postnecrotic cirrhosis was thrombosis of the portal vein, aneurysmal dilatation of the right branch of the portal vein, and rupture of this aneurysm into the common bile duct, producing a hemocholecyst.

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REPORT OF CASE

A white woman, aged 21 years, was admitted to Ochsner Foundation Hospital on Dec. 29, 1953, because of massive gastrointestinal hemorrhage several weeks before.

During early childhood the patient and two of her brothers had had hepatitis simultaneously. One of the brothers died in 1950 from ruptured esophageal varices and cirrhosis, presumably posthepatitic.

Physical examination at the time of admission revealed an enlarged spleen. Esophagoscopy disclosed huge varices. A diagnosis of postnecrotic cirrhosis, splenomegaly, esophageal varices, and pancytopenia secondary to hypersplenism was established.

In January, 1954, splenectomy only was performed, but, because no significant improvement in the platelet count, bleeding time, and hepatic flocculation occurred, portacaval shunt was not recommended at this time. The portal venous pressure dropped from 440 mm. of water prior to splenectomy to 310 mm. of water subsequently. The spleen weighed 1510 gm. At the time of the patient's discharge from the hospital two months later, a roentgenogram of the esophagus showed considerable reduction in the size of the varices. Reevaluation of the clinical course in April and July, 1954, during which time she was following a Patek regimen, disclosed slight improvement in the results of hepatic flocculation tests, serum proteins, hemogram, and prothrombin time.

On Dec. 4, 1954, the patient was readmitted to Ochsner Foundation Hospital because of severe substernal pain, jaundice, light colored stools, dark urine, and weakness. Four weeks prior to this, she had had an acute infection of the upper respiratory tract. Jaundice developed three weeks later. Two days before admission, the patient complained of steady, lancinating substernal pain. She vomited a small amount of coffee-ground material twice on the day of admission.

Physical examination disclosed a critically ill patient with jaundice, generalized pruritus, exquisite tenderness and guarding over the lower sternal and epigastric regions, spider angiomas, palmar erythema, ecchymoses, pedal edema, and evidence of dehydration. The liver was not palpable.

Laboratory studies at this time revealed the following abnormalities: hemoglobin, 7 gm. per 100 cc. of blood; hematocrit value, 36%; erythrocyte count, 3,640,000 per cubic millimeter; pronounced anisocytosis, poikilocytosis, and hypochromasia; leucocyte count, 19,600 per cubic millimeter; 86% neutrophiles; slight albuminuria and pronounced biliuria; positive guaiac reaction of the stool; serum amylase, 1600 units (Somogyi) (normal 85 to 200 units); serum lipase, 1.4 units (normal, 1.2 units); direct and indirect serum bilirubin, 17.6 mg. and 9.6 mg. per 100 cc.; serum albumin and globulin, 2.9 gm. and 2.3 gm. per 100 cc.; blood urea nitrogen, 10 mg. per 100 cc., and prothrombin time, 11 seconds (normal 15 seconds). The serum values for electrolyte-battery, cephalin-cholesterol flocculation, and thymol turbidity were normal. A diagnosis of postnecrotic cirrhosis, hepatic insufficiency, ruptured esophageal varices, and acute pancreatic necrosis was established.

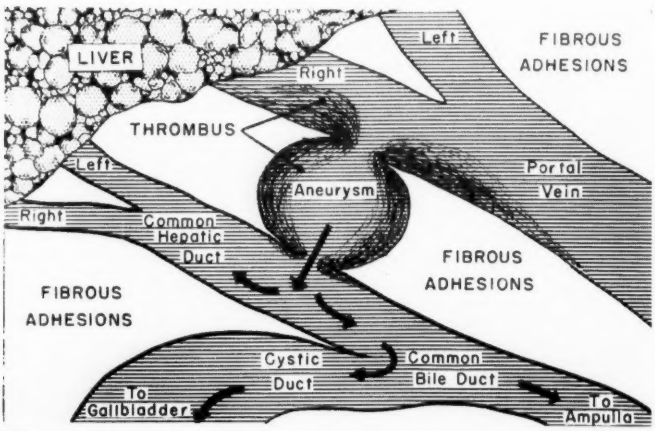
On Dec. 8, massive hematemesis necessitated institution of pneumatic esophagogastric tamponade and several transfusions of blood. Subsequently, though melena persisted, deflation of the esophageal balloon was accomplished without further hematemesis.

On Dec. 13, a firm, globular mass was palpated in the right subcostal area. The size of the mass appeared to fluctuate for the next several days. Because it was suspected of being a distended gallbladder, cholecystostomy was performed with use of local anesthesia. The gall bladder was distended by thick bile and clotted blood. Postoperatively, blood drained continuously from the cholecystostomy tube, and melena persisted. On Dec. 21, the patient suddenly became comatose and died several hours later.

Permission was granted only for postmortem examination of the abdominal viscera. There was a minimal amount of ascitic fluid in the peritoneal cavity. The liver weighed 2550 gm. and was grayish-pink. The surface of the liver was studded with irregularly shaped, coarse nodules, typical of postnecrotic cirrhosis. A distended gall bladder projected 10 cm. below the inferior margin of the liver. It contained about 100 cc. of clotted and partially clotted blood. The entire hepatic and common bile ducts contained blood. An extensive network of collateral veins surrounded the hepatobiliary system. The portal vein was dilated about 3 cm. There was a recent thrombus in the right branch of the portal vein, partially occluding its lumen. Near the middle third of the thrombus, the wall of the vein had a saccular aneurysm measuring about 2 cm. in diameter. This aneurysm contained clotted blood and communicated directly with the common hepatic duct, about 1 cm. above the junction of the cystic duct (Figure). The common bile duct measured 2 cm. in diameter. Two small superficial erosions were found in the huge varices of the lower portion of the esophagus. The stomach, small intestine, and colon were greatly congested and contained a large amount of blood. The pancreas was congested but otherwise appeared normal.

The salient histologic observations of the abdominal viscera included (1) necrosis of hepatic cells, broad zones of fibrous connective tissue, regenerative nodules, and bile pigment in the pseudolobules; (2) esophageal varices and erosion of the esophageal mucosa; (3) chronic passive congestion of the stomach, small intestine, pancreas, and colon; (4) organized thrombus of the splenic vein; (5) recent thrombus of the portal vein, and (6) congestion and necrosis of the epithelium of the gall bladder.

The pathologic diagnoses were postnecrotic cirrhosis, esophageal varices, aneurysm of the portal vein with rupture into the common hepatic duct, intracholedochal hemorrhage, and hemocholecyst.



Diagrammatic representation of the postmortem observations showing the portal vein aneurysm, its rupture into the common hepatic duct, and its relationship to the surrounding structures

COMMENT

This case of postnecrotic cirrhosis merits attention for several reasons. Massive hemorrhage into the biliary tract resulting in a hemocholecyst followed rupture of an aneurysm of the portal vein into the common hepatic duct. To our knowledge this mechanism producing a clinically significant hemocholecyst has not been previously described. As this case illustrates, Courvoisier's law is mimicked by a hemocholecyst occurring in a patient with jaundice. Actually, it was originally assumed that the patient had obstructive jaundice and a distended gall bladder as the result of acute pancreatic necrosis. It was noted that inflation and deflation of the gastric partition of the pneumatic esophagogastric balloon was associated with an increase or decrease, respectively, of the hemocholecyst. It is conceivable that tamponade of the esophageal and gastric varices may be reflected in an increase in pressure in the partially thrombotic portal vein, the portobiliary aneurysm, the extrahepatic bile ducts, and the gall bladder.

Clinically, unexplainable melena persisted despite seemingly adequate esophagogastric tamponade. Hypoprothrombinemia, thrombocytopenia, hypofibrinogenemia, and hemorrhagic gastritis frequently observed in advanced cirrhosis may play a role in gastrointestinal hemorrhage.[9] However, this case represents that type of continued gastrointestinal bleeding which may persist, in addition, because of massive hemorrhage into the extrahepatic biliary ducts and consequently into the duodenum. In view of the relatively normal appearance of the pancreas at necropsy, it is assumed that severe upper abdominal pain, jaundice, and gastrointestinal hemorrhage were clinical manifestations of intracholedochal hemorrhage. This represents an unusual mechanism for persistent gastrointestinal hemorrhage. The significantly elevated values of serum amylase and lipase then lead one to suspect that channeling of the blood from the common bile duct into the main pancreatic duct had produced pancreatitis. The histopathologic evidence of acute pancreatic necrosis or the nonspecific pancreatic lesions observed in cases of cirrhosis, nevertheless, were not identified at necropsy. In addition, thrombosis of the portal vein is not uncommonly observed in cases of cirrhosis.[10] The absence of ascites, despite portal hypertension in our case, correlates well with the recent concept of ascites in cirrhosis.[11]

SUMMARY

A case of postnecrotic cirrhosis with persistent gastrointestinal hemorrhage as the result of aneurysmal rupture of a thrombotic portal vein into the extrahepatic bile ducts is described. To our knowledge this mechanism producing a clinically significant hemocholecyst has not been previously reported. A hemocholecyst was produced from the intracholedochal hemorrhage and masqueraded as "Courvoisier's gall bladder."

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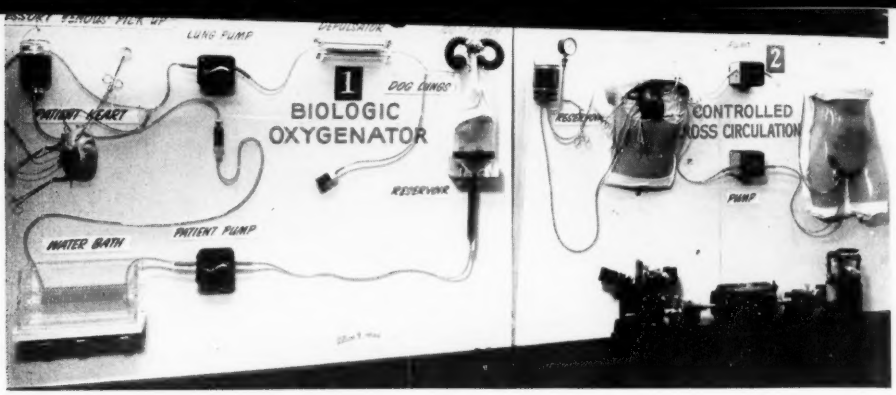

Scientific Exhibits

DIRECT VISION INTRACARDIAC SURGICAL CORRECTION OF CONGENITAL HEART DEFECTS

C. WALTON LILLEHEI, M.D.; MORLEY COHEN, M.D.; HERBERT E. WARDEN, M.D.; RAYMOND C. READ, M.D.; JOSEPH B. AUST, M.D.; RICHARD A. DeWALL, M.D.; NEWELL R. ZIEGLER, M.D.; GILBERT S. CAMPBELL, M.D.; E. B. BROWN, M.D.; NORMAN CRISP, M.D., and RICHARD L. VARCO, M.D., Minneapolis

This exhibit describes three different methods developed in our experimental laboratory and successfully applied in man for total by-pass of the heart and lungs to allow direct vision intracardiac surgical correction of congenital or acquired heart defects which heretofore were either not operable or subject to palliative procedures only.

These methods are (1) controlled cross circulation, (2) heterologous lung oxygenator, and (3) continuous arterial perfusion from a reservoir of oxygenated blood.

The following types of congenital cardiac malformations—ventricular septal defects, atrioventricularis communis, isolated infundibular pulmonic stenosis, and tetralogy of Fallot—have been successfully treated by direct vision intracardiac correction of the anatomic defect or defects present, thereby restoring the circulation to normal.

From the Department of Surgery, University of Minnesota Medical School.

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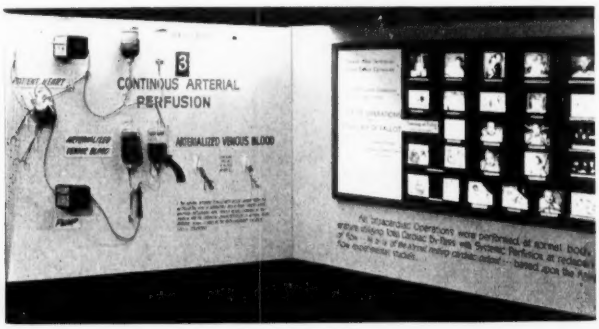


THE METHODS IN MAN

Controlled Cross Circulation

Figure 1 illustrates diagrammatically the method of linking together the circulatory systems of the patient and the donor for the reciprocal exchange of arterial and venous blood, permitting the heart and lungs of the patient to be totally by-passed for sufficient intervals to allow definitive surgery under direct vision.

For the exposure of the heart and great vessels the patient has been placed in a supine position upon the operating table and the chest is entered through an anterior bilateral thoracotomy incision in the fourth interspace dividing the sternum transversely.

After incision of the pericardium the caval entrances at the auricle are dissected from their adjacent tissues cardiac to the azygos and hepatic veins respectively. Cotton tapes are then passed around these veins as indicated to permit complete venous inflow stasis during the cardiotomy.

Cannulations in the Patient.—The patient's venae cavae are cannulated by individual plastic catheters of small caliber (12-14 F.) inserted through separate stab wounds in the right atrium and then joined by a stainless steel Y-adaptor.

The arterial blood is returned to the patient via a similar-sized catheter inserted into the central end of the subclavian artery.

Donor Cannulations.—The donor cannulations have been performed through a short incision 2 fingerbreadths below either the right or the left inguinal ligament exposing the great saphenous vein and the superficial femoral artery. The donor's venous catheter has been threaded into the saphenous vein so that its tip lies in the iliac vein or inferior vena cava. The donor's arterial catheter has been inserted into the superficial femoral artery through a small incision and is positioned so that its multiple-holed tip lies within the abdominal aorta.

Anticoagulants.—Just prior to the insertion of these catheters, both donor and patient are given a single intravenous dose of heparin (0.75 mg. per pound of body weight).

Venous Reservoir and Bubble Trap.—The venous reservoir (Fig. 1) serves two important functions, each of which augments the safety of the controlled cross circulation method. The first of these functions is to maintain a free flow of blood out of the patient's caval system under all conditions by preventing the development of an elevated negative pressure in the afferent venous circuit which tends to occlude the catheter tips by causing the thin caval walls to be sucked into the catheter ostia. The second important function of the reservoir is to serve as an effective bubble trap.

The Pump.—An efficient pump is the only special equipment required for the performance of intracardiac surgery by these techniques.

The pumping unit * common to all of these techniques consists of a single explosion-proof electric motor (⅓ h. p.) which activates two pumps, each equipped with an individual speed changer and gear box all mounted on a single base (Fig. 1). The entire unit weighs about 75 lb. The flows in the two circuits can

* Sigmamotor Model T-6S, 3 North Main, Middleport, N. Y.

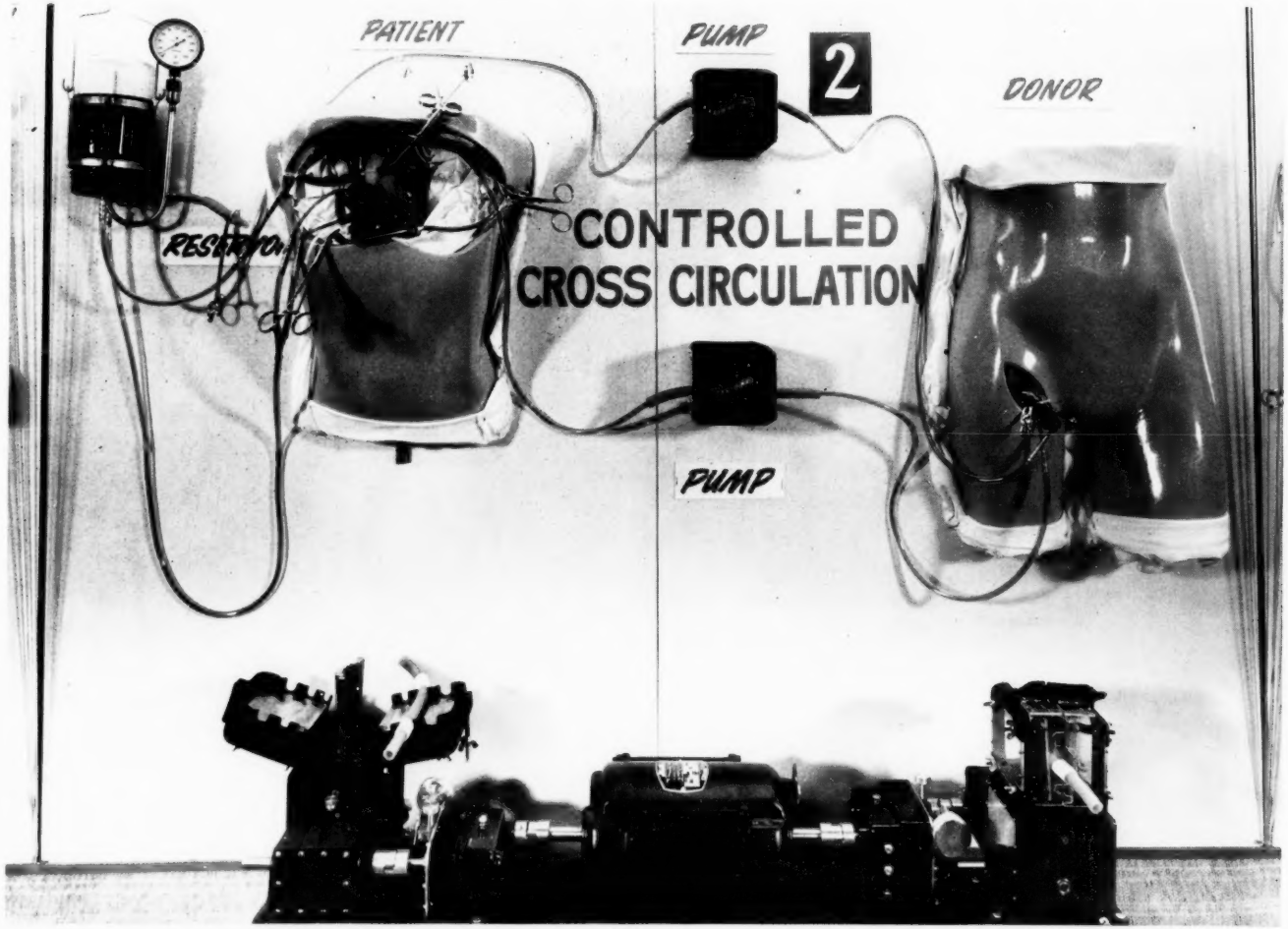


Figure 1

be quickly balanced by a vernier adjustment of the speed control. The rate of flow is determined by adjustment of the speed changer and the size of tubing used.

The top of the pump casing is hinged (Fig. 1) to allow easy insertion of the heat-sterilized tubing. The two halves of the top open, and the tubes are inserted in their proper slots in the side plates. The halves are then closed around the tubes and locked in place.

Selection of Donors.—None of the patients or donors undergoing the cross circulation procedure have exhibited any evidence of blood incompatibility reactions. The complete freedom from this complication emphasizes the rewards of careful typing and cross matching of the patient's, donor's, and citrated bank blood utilized for loss replacement.

In addition to a determination of the better-known cell types, both a saline centrifugal and an indirect Coombs' cross match are performed upon all blood to be mixed.

Results.—Controlled cross circulation was the initial method developed for direct vision intracardiac correction of these defects and has been utilized sufficiently to date to permit evaluation of the results of its application to lesions previously not amenable to curative surgery.

These results in the first 41 patients operated upon in the period beginning March 26, 1954, through April, 1955, are listed in Figure 2.

Figure 1

RESULTS OF

Direct Vision Intracardiac Surgery

by means of controlled cross circulation

PATIENT PATHOLOGY	CORRECTIVE OPERATION	NO. CASES	DEATHS	NO. ESCATEL-BAZZED	NO. CURED
VENTRICULAR SEPTAL DEFECT	SUTURE CLOSURE OF DEFECT	26	7	5	5
TETRALOGY OF FALLOT	SUTURE CLOSURE OF IVSD AND RESECTION OF INFUNDIBULAR STENOSIS	10	4	2	*2
ATRIOVENTRICULARIS COMMUNIS	SUTURE CLOSURE OF BOTH ATRIAL AND VENTRICULAR DEFECTS WITH CORRECTION OF VALVULAR DEFORMITY	3	2	1	1
ISOLATED INFUNDIBULAR PULMONIC STENOSIS	RESECTION OF INFUNDIBULUM	1	0	1	1
PULMONARY STENOSIS PLUS I.A.S.D. AND ANOMALOUS PULMONARY DRAINAGE	VENTRICULAR AND ATRIAL CARDIOTOMIES, TRANSPOSITION OF PULMONARY VEINS	1	1		

DONOR RESULTS

Number 41 Mortality 0

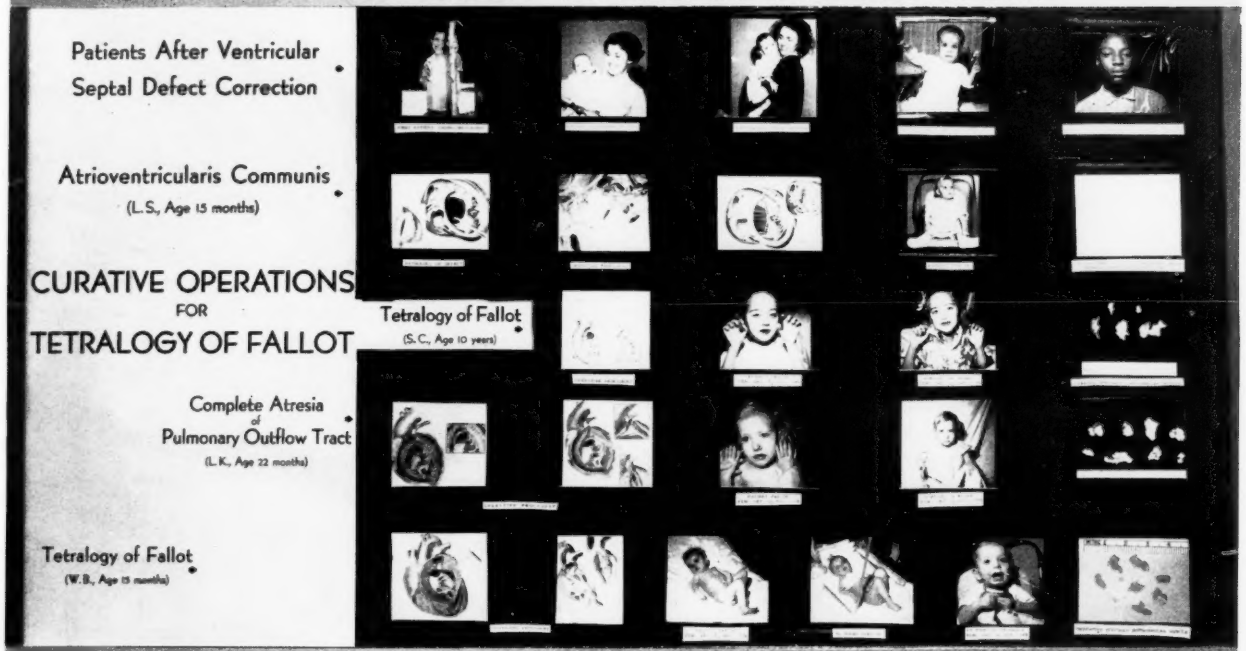
One serious donor complication—profound hypotension requiring thoracotomy ··· complete recovery

*A small I.P.S. Shunt remains in one patient otherwise asymptomatic

Figure 2

REPRESENTATIVE PATIENTS

CORRECTED BY OPEN INTRACARDIAC SURGERY


Patients After Ventricular Septal Defect Correction
Atrioventricularis Communis
(L.S., Age 15 months)
CURATIVE OPERATIONS FOR TETRALOGY OF FALLOT
Tetralogy of Fallot
(S.C., Age 10 years)
Complete Atresia of Pulmonary Outflow Tract
(L.K., Age 22 months)
Tetralogy of Fallot
(W.B., Age 15 months)

All Intracardiac Operations were performed at normal body temperature utilizing Total Cardiac By-Pass with Systemic Perfusion at reduced rates of flow ··· *¼ to ⅛ of the normal resting cardiac output* ··· based upon the Azygos flow experimental studies.

Continuous Arterial Perfusion Utilizing Arterialized Venous Blood

The above-mentioned clinical experience gained with cross circulation emphasized the fact that, especially in infants or small children, relatively small volumes of arterial blood were sufficient to support the patient during the period of perfusion. Hence the development of the reservoir method of perfusion depicted in Figure 4. It may be noted that the general plan is similar to that employed in the controlled cross circulation method described above with the exception that the donor is replaced by arterial and venous reservoirs. These are standard siliconized blood collection bottles (500 cc. or 1,000 cc.).

An important contribution to the simplicity and convenience of collection of arterial blood for these procedures has been the use of arterialized venous blood collected, as depicted in the insert in Figure 5, from compatible donors whose arms have been warmed at 45 C for 15 minutes prior to collection in water. Then by means of a venepuncture in the antecubital fossa, 500 cc. of arterialized venous blood is collected by gravity from each of the donors. The collections are carried out in the blood bank by the regular technicians delegated for blood collection duties.

This technique for intracardiac surgery, because of its simplicity and physiologic soundness, has been particularly adaptable for open cardiotomy in infants and small children. The lack of unlimited operating time has not proved to be a serious obstacle in selected cases.

Total Cardiac By-Pass Utilizing Heterologous (Canine) Lungs as Biologic Oxygenators

The method for intracardiac surgery of by-passing the heart and using dog lungs as oxygenators has the advantage of relative simplicity, no donor individual is needed, and relatively unlimited operating time is available to the surgeon.

The extracorporeal circuit is diagrammatically presented in Figure 5. The patient's cannulations are identical with those previously described.

The lungs are removed from a healthy heparinized dog under aspetic conditions. A plastic cannula is inserted into the main pulmonary artery of these lungs and the lungs are perfused with sterile 6% dextran until they become "chalk white" in color (i. e., all of the dog's blood is removed). Subsequently the lungs are attached to the all plastic extracorporeal circuit as depicted in Figure 5.

During the cardiac by-pass, venous blood is aspirated from the patient's superior and inferior vena cavae and circulated via the "lung pump" through the depulsator and thence into the pulmonary artery of the isolated dog lungs. The lungs are ventilated with 100% oxygen at an intermittent positive pressure insufflation of 14 to 18 cm. of water pressure at a ventilatory rate of 12 to 14 times per minute.

Fully oxygenated blood passes via the open, noncannulated pulmonary veins into the plastic lung housing chamber and is aspirated by the "patient pump." This oxygenated blood is pumped then by the "patient pump" through the water bath (38-40 C.), through the plastic blood filter, and into the patient's aorta via his subclavian artery.

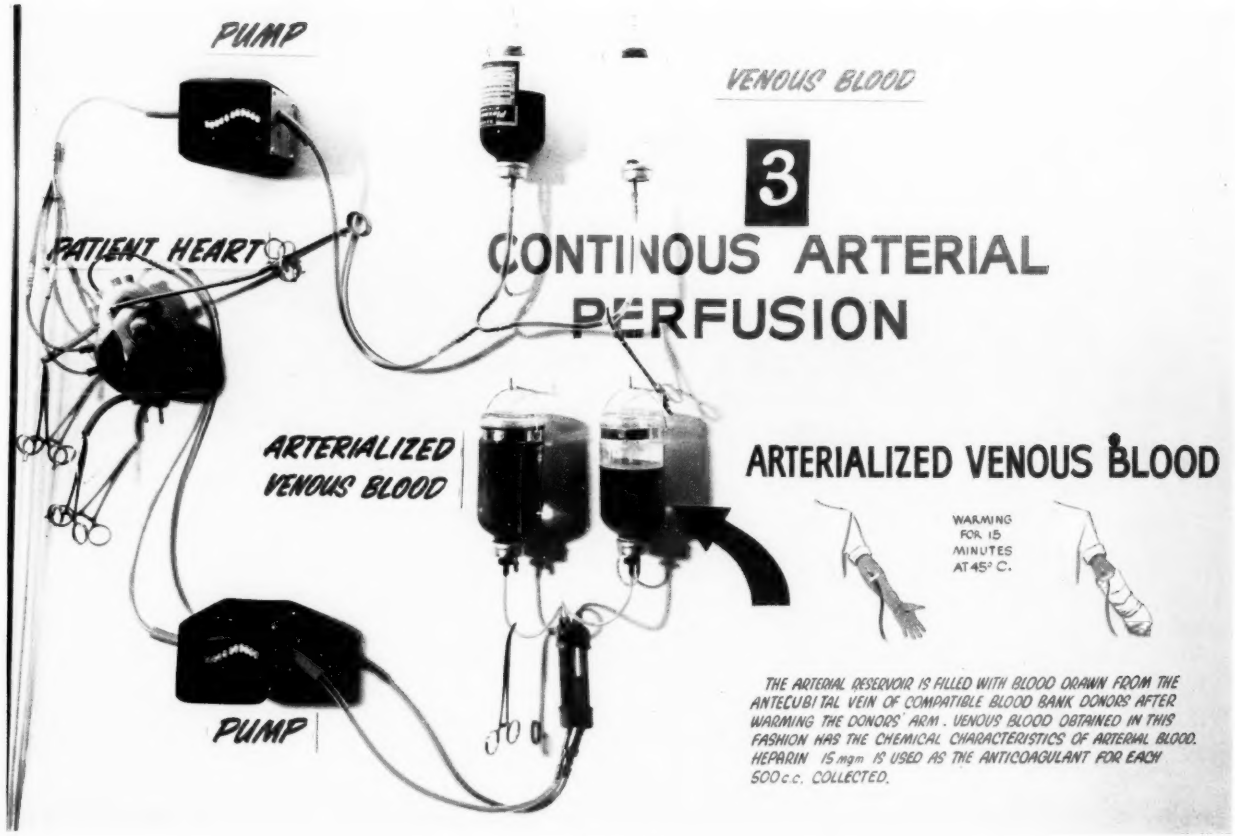

PUMP
VENOUS BLOOD
3
PATIENT HEART
CONTINOUS ARTERIAL
PERFUSION
ARTERIALIZED
VENOUS BLOOD
ARTERIALIZED VENOUS BLOOD
WARMING
FOR 15
MINUTES
AT 45° C.
THE ARTERIAL RESERVOIR IS FILLED WITH BLOOD DRAWN FROM THE ANTECUBITAL VEIN OF COMPATIBLE BLOOD BANK DONORS AFTER WARMING THE DONORS' ARM. VENOUS BLOOD OBTAINED IN THIS FASHION HAS THE CHEMICAL CHARACTERISTICS OF ARTERIAL BLOOD. HEPARIN 15 mgm IS USED AS THE ANTICOAGULANT FOR EACH 500 c.c. COLLECTED.
PUMP

Figure 4

Venous aspiration from the patient can be dynamically equated with arterial return to the patient by observing the blood level in the plastic lung housing and adjusting the speeds of the appropriate pump as necessary.

Human blood has been perfused by these means through the isolated dog lungs at a normal pulmonary artery perfusion pressure and at a flow of 400 to 650 cc. per minute for 30 to 90 minutes without any evidence of pulmonary edema or congestion in the isolated lungs. Pulmonary artery pressure in the isolated dog lung is always monitored during the lung perfusion and is preferably held below 30 mm. of mercury.

In addition to its use in patients with congenital cardiac defects, this method has been successfully utilized for the surgical correction, by open cardiotomy, of a traumatic ventricular septal defect in a 15-year-old boy of adult size (Fig. 3, top row far right).

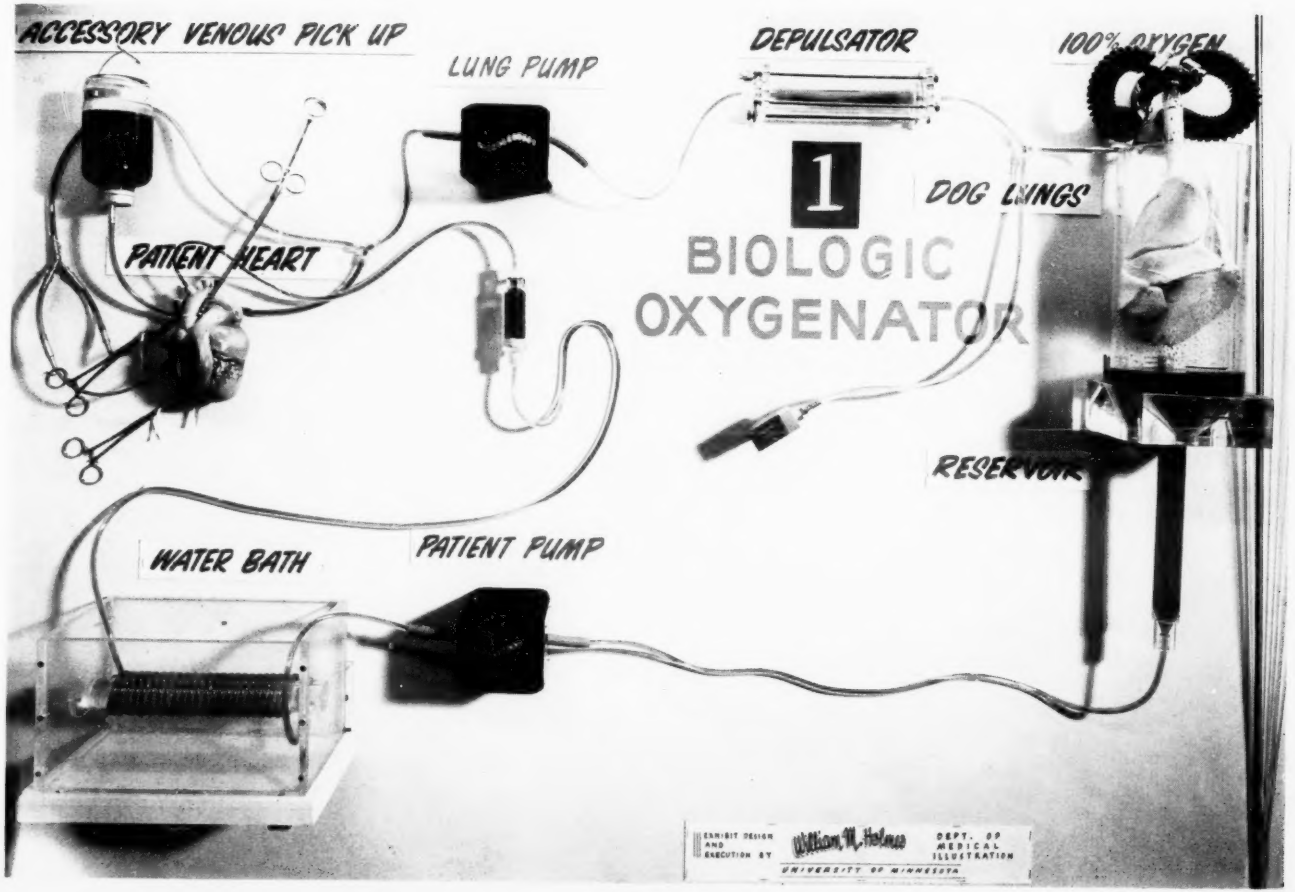

ACCESSORY VENOUS PICK UP
LUNG PUMP
DEPULSATOR
100% OXYGEN
1
DOG LUNGS
PATIENT HEART
BIOLOGIC
OXYGENATOR
RESERVOIR
WATER BATH
PATIENT PUMP
EXHIBIT DESIGN AND EXECUTION BY
William M. Holmes
DEPT. OF MEDICAL ILLUSTRATION
UNIVERSITY OF MINNESOTA

Figure 5

Figure 5